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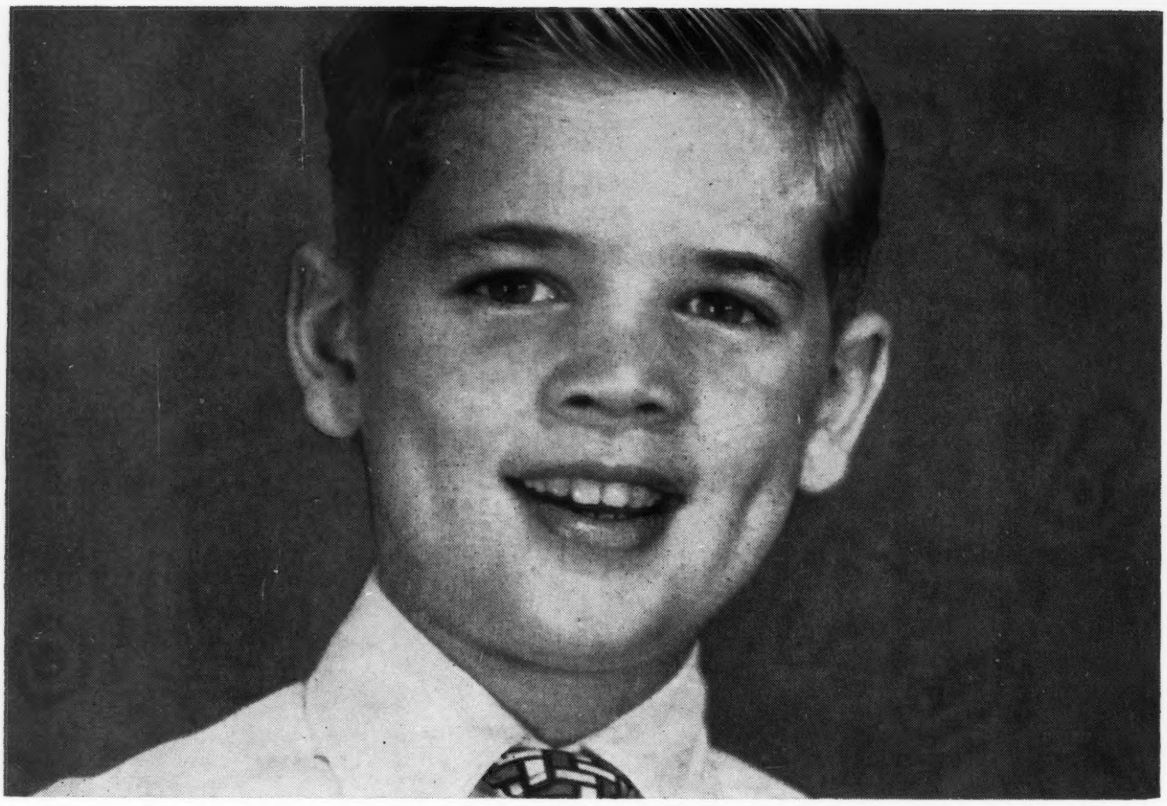
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1. Means, J.H.: The Thyroid and Its Diseases, ed. 2. Philadelphia, J.B. Lippincott Co., 1948.

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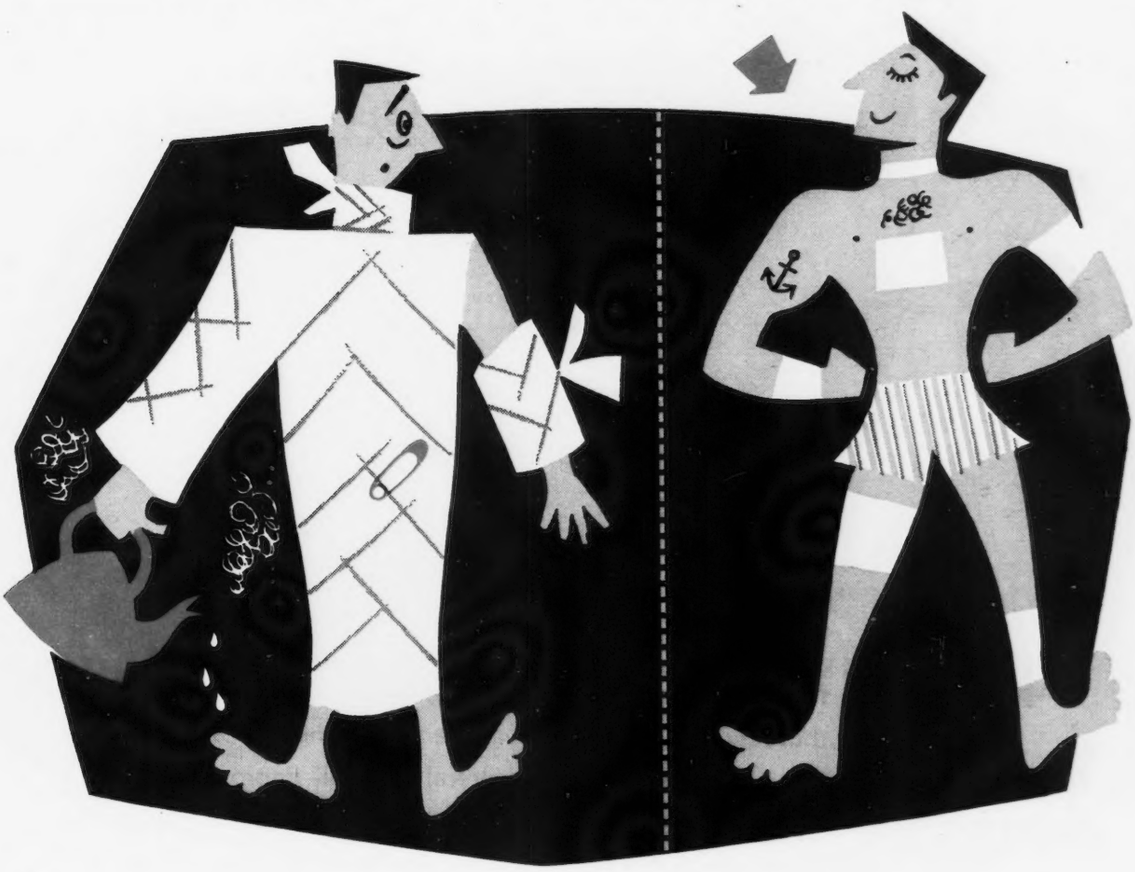
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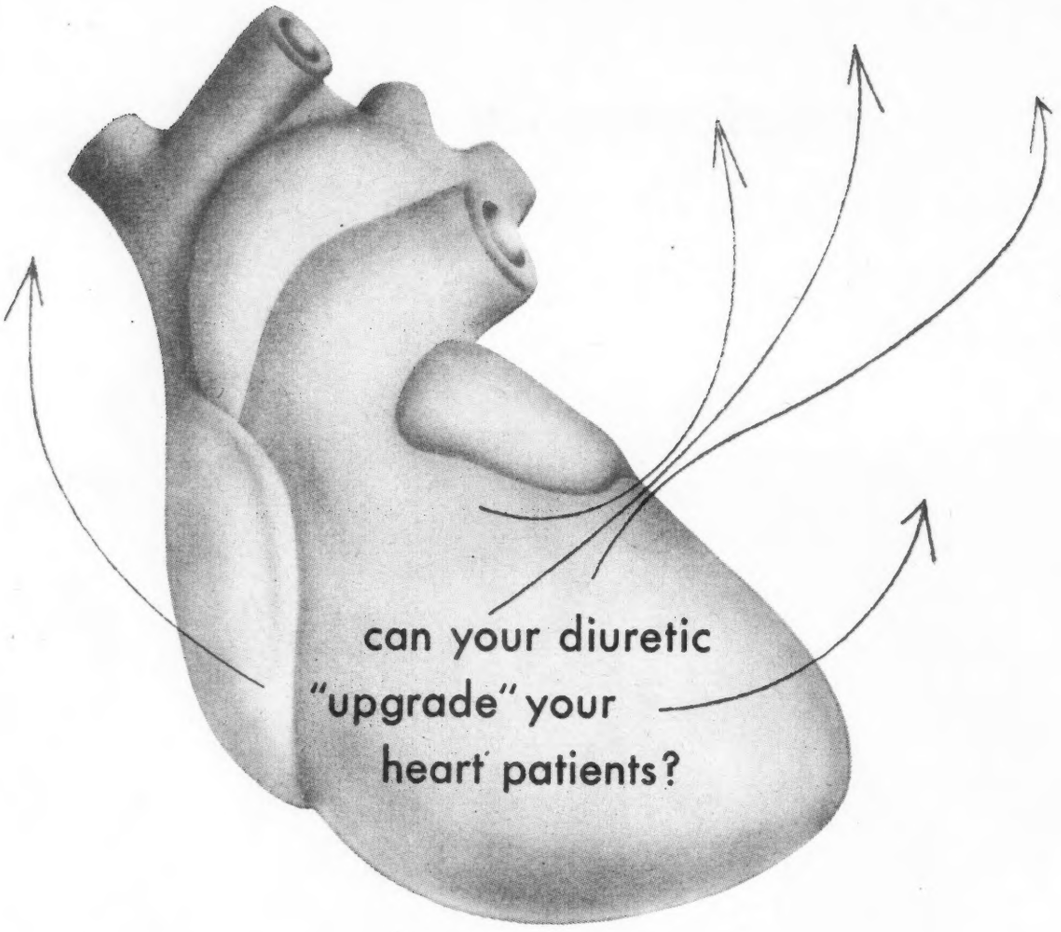
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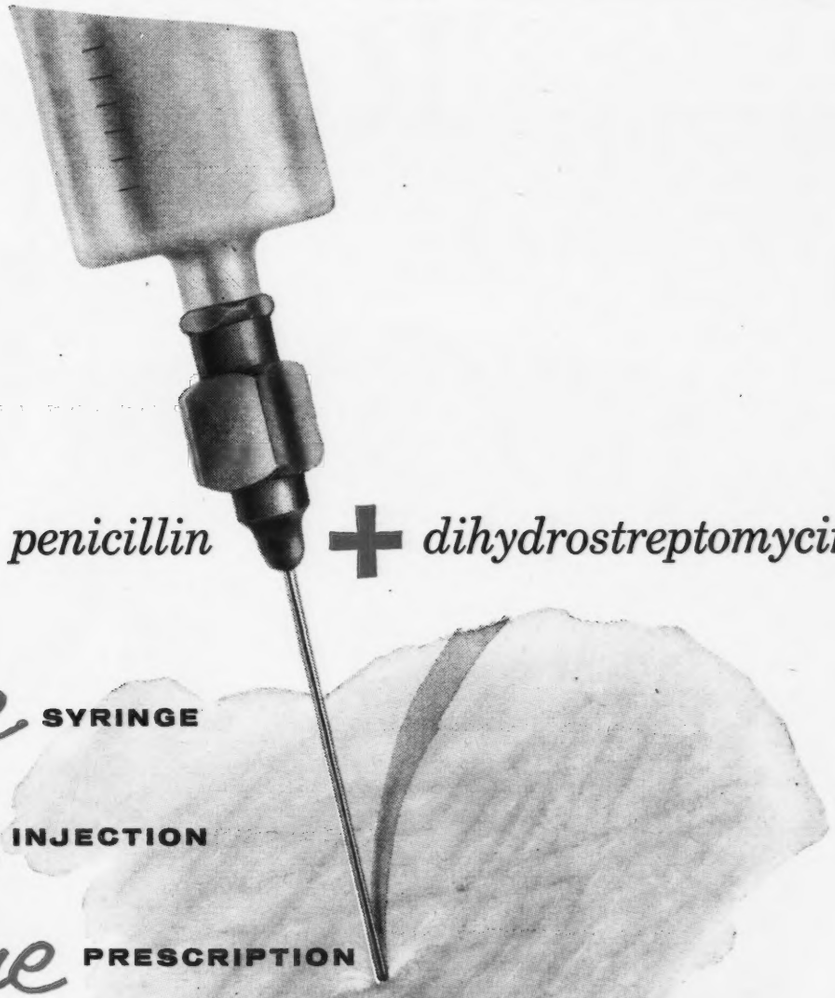
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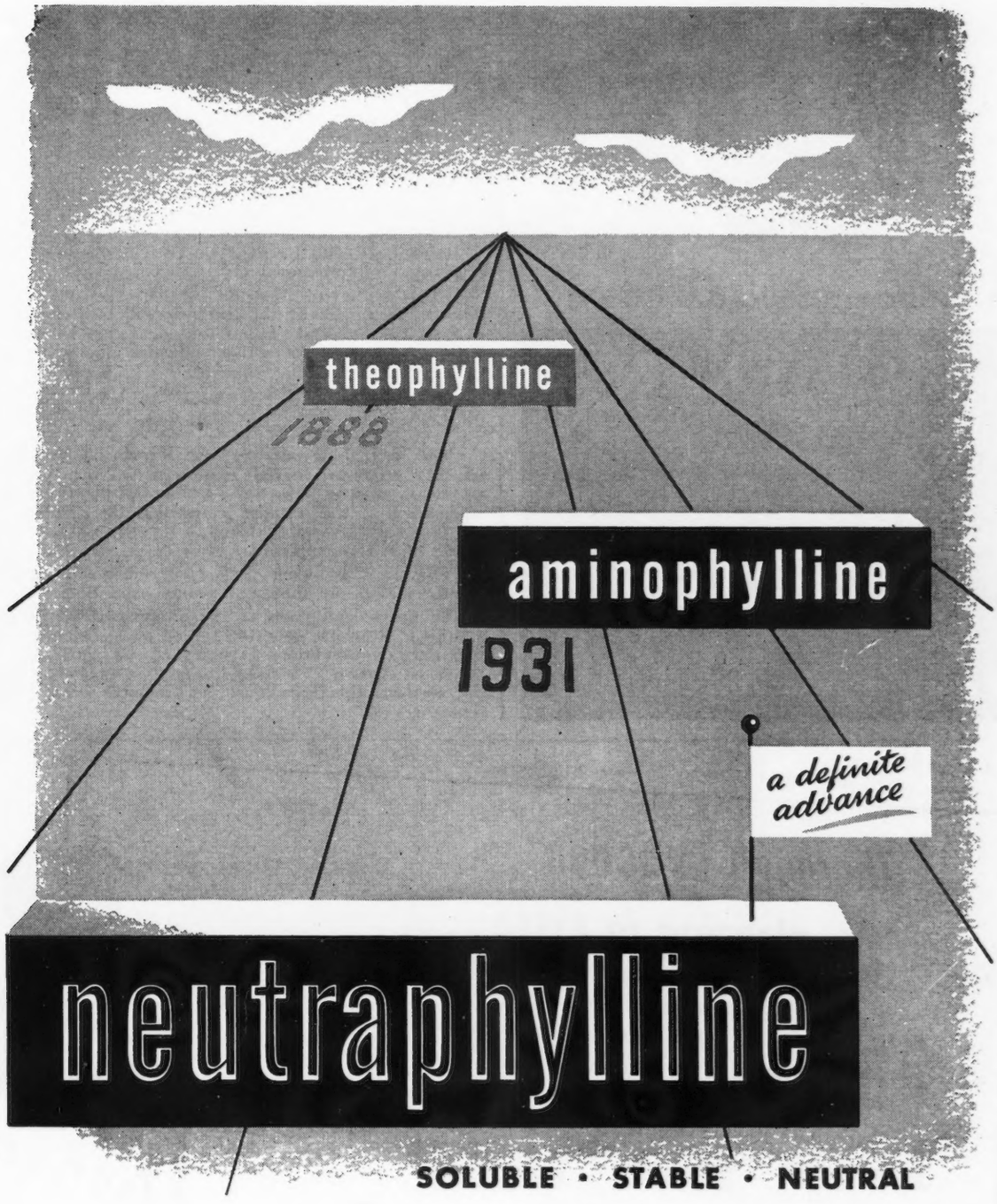
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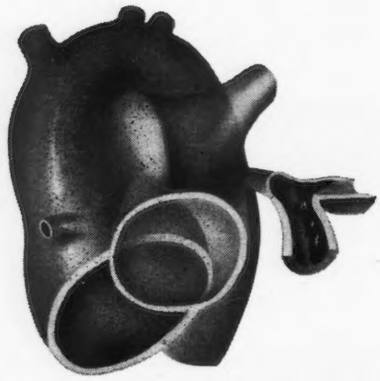


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From the Journal of April, 1926

Three great health organizations in Canada are combining forces to hold a unique national health congress in Toronto early in May.

This congress will represent the joint strength and points of view of the Ontario Health Officers' Association, the Canadian Public Health Association and the Canadian Social Hygiene Council.

By special arrangement, the Academy of Medicine, Toronto, has invited all the visiting physicians to meet with them at the Academy on the evening of May 6, when the question of "Periodic Health Examination" will be discussed from both national and international angles.

Other matters of great interest to the general public which will be dealt with by the congress will be "Medical Aspects of Immigration" and "Immunization against Disease," one of the latest phases of preventive medicine.

Nova Scotia

The annual reports of the Provincial Health Officer recently presented to the legislature of Nova Scotia contain much of interest. In that dealing with public health, a comparison of the counties shows that the greatest statistical improvement has been effected in those counties where public health nurses are employed.

The press is being used for educational purposes and health exhibits are shown at county exhibitions, etc.

To the several gaols of the province 1,803 persons were admitted, of whom only 146 served gaol sentences exceeding two months. Conditions in many of the gaols are far from being satisfactory. The desirability of a prison farm to serve the needs of the three Maritime provinces is set forth in the report.

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1. Donegan, J. M. and Thomas, W. A., Capillary fragility and cutaneous lymphatic flow in relation to systemic and retinal vascular manifestations: rutin therapy, Am. J. Ophth., 31:671, 1948.

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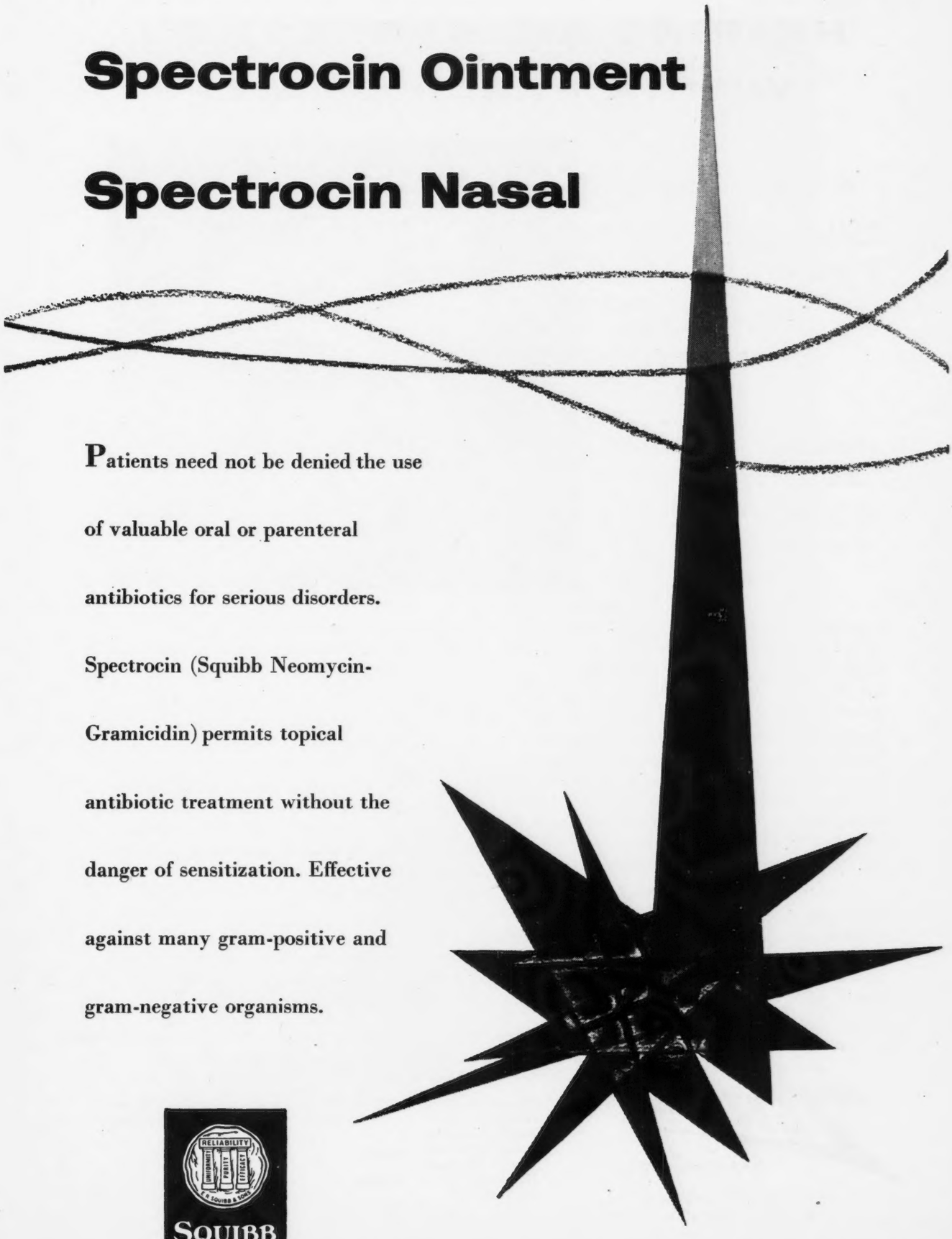
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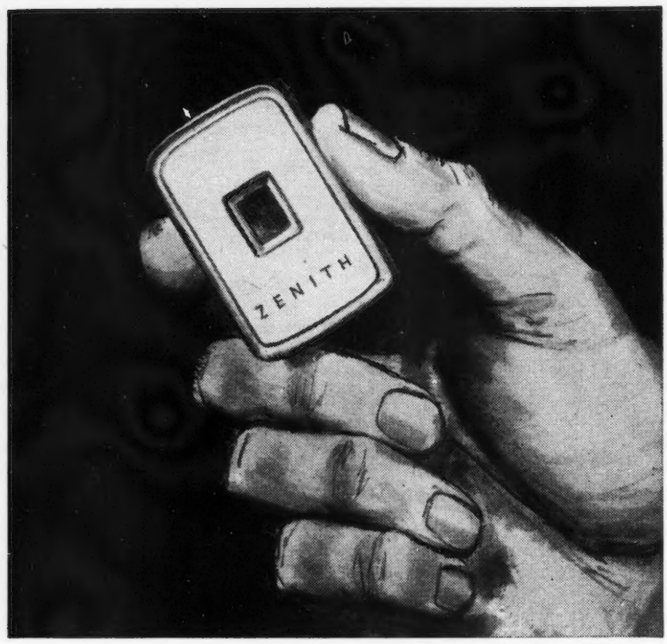
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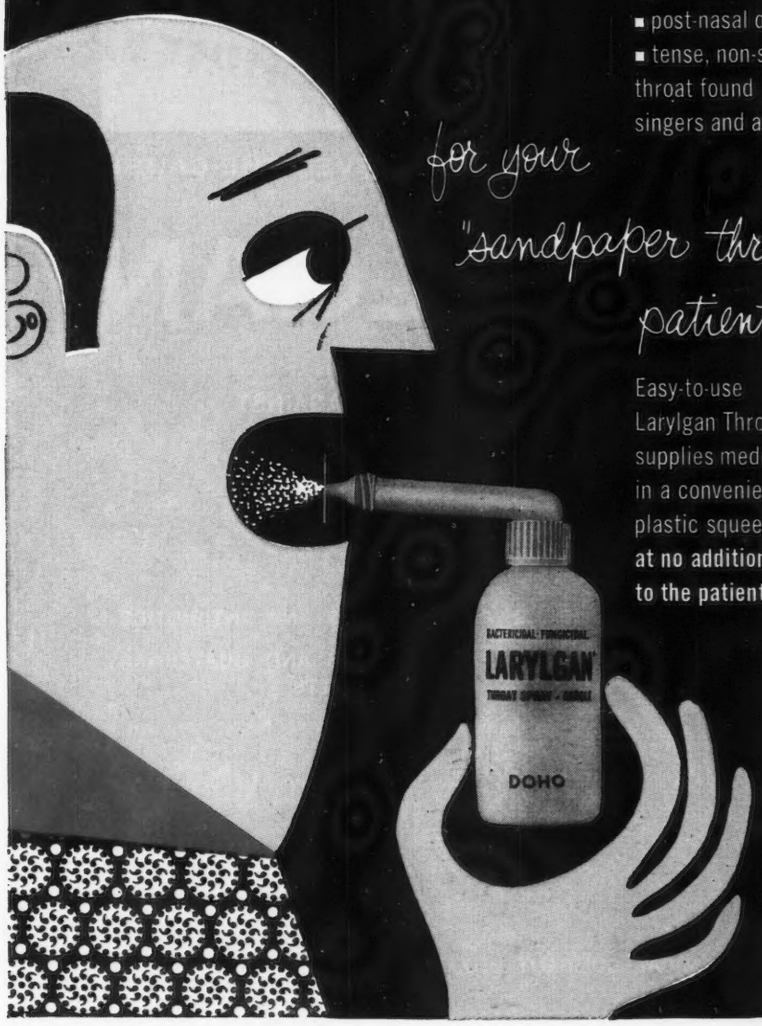
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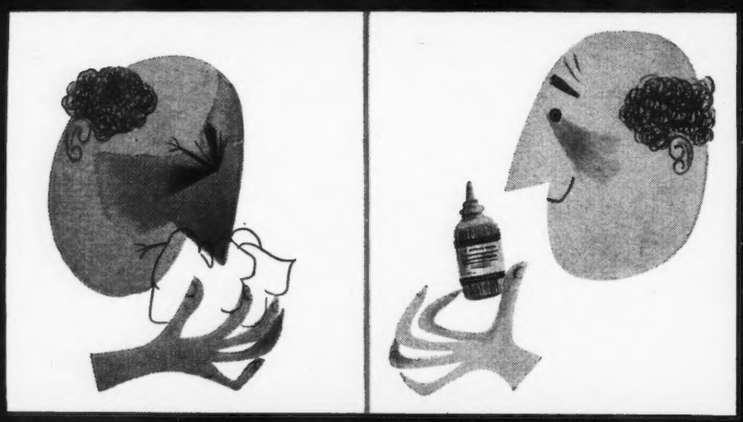
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3. minimize feminizing and gastrointestinal side reactions of estrogen therapy.

MECHANISM OF ACTION

Although still inconclusive, laboratory evidence and extensive clinical studies in Europe and Canada suggest the following mechanism operates. Stilbestrol diphosphate sodium is essentially a "transport form" of stilbestrol. The compound is water-soluble, well-tolerated, and pharmacologically inert at injection. It becomes activated preferentially in malignant prostatic tissue because of the high level of phosphatase activity there. On reaching the prostate, the phosphate groups are removed from the Honvol molecule by the enzyme phosphatase, and active stilbestrol is released directly in the tumour and its metastases.

Such localization of high stilbestrol concentrations specifically in malignant prostatic tissue makes possible a degree of cytotoxic action unobtainable with other hormone therapy.

TARGET SELECTIVITY

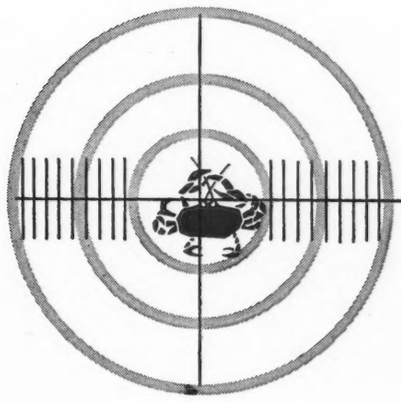
This release of stilbestrol presumably can take place wherever phosphatases are present. But the uniquely high levels of this enzyme in carcinatomous prostatic tissue assure target selectivity with virtual absence of systemic hormonal effects. This has certainly been borne out in the clinical studies *where feminizing effects have been rare and minor.*

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Stilbestrol Diphosphate Sodium, 250 mg.
For intravenous use only.

CLINICAL RESULTS

The results of clinical studies are too extensive for outline here. They are available from Frank W. Horner Limited. But it can be said that the rapid improvement of prostatic carcinoma —both clinically and biochemically—with negligible side effects—makes Honvol therapy very heartening. In particular, it offers real hope in those cases which have become refractory to castration and present-day hormone control methods.



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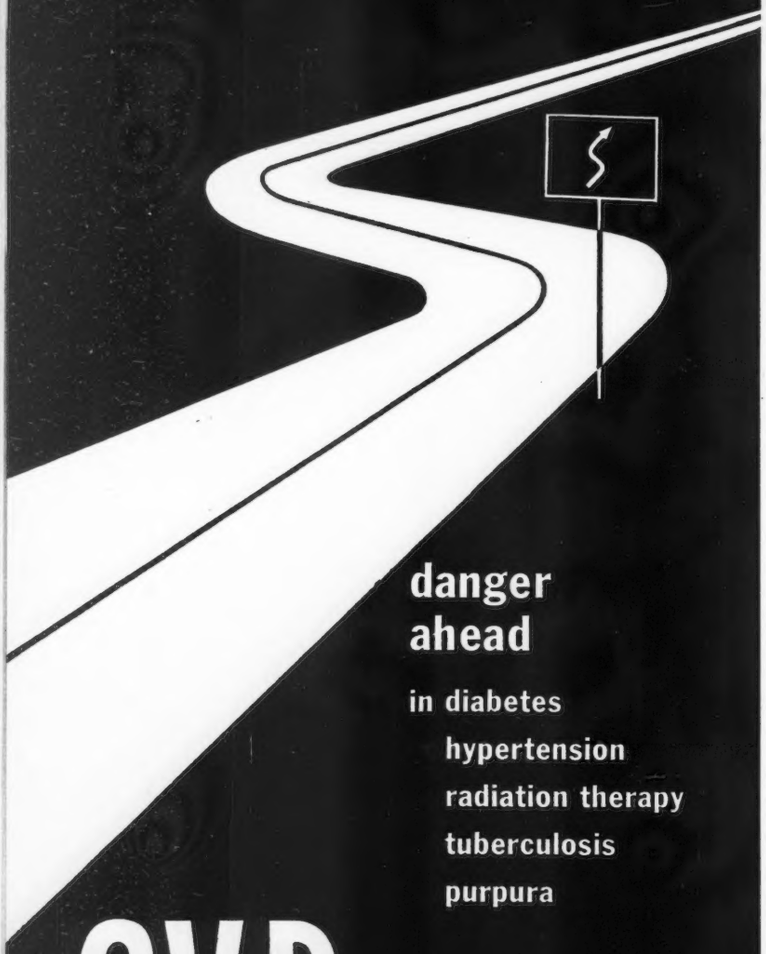
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(1) Dickson, R.M.: Brit. J. Ophth. 26:529, 1942.
(2) Collier, E.: Brit. J. Phys. Med. 6:181, 1943.
(3) Dickson, R.M.: Brit. J. Phys. Med. 7:77, 1944.
(4) Kuhn, H.S.: Tr. Am. Acad. Ophth. 55:431, 1951.

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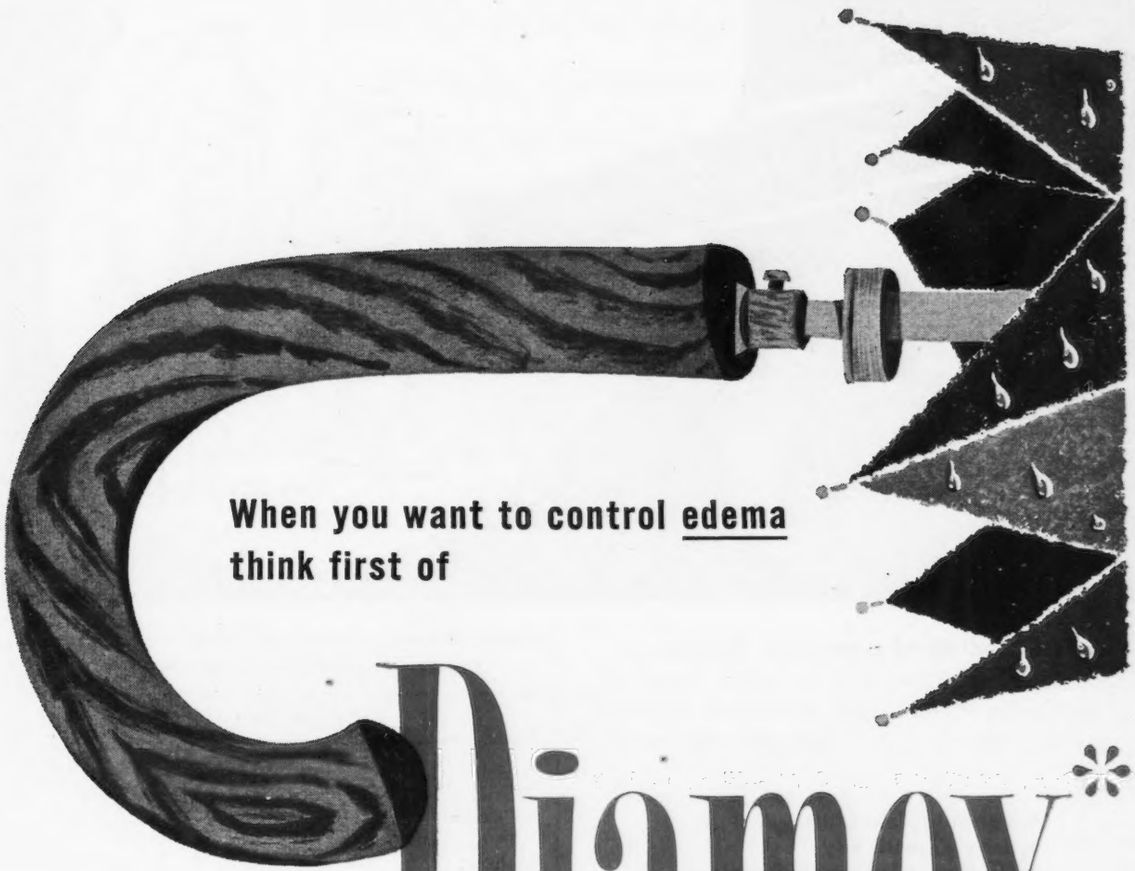
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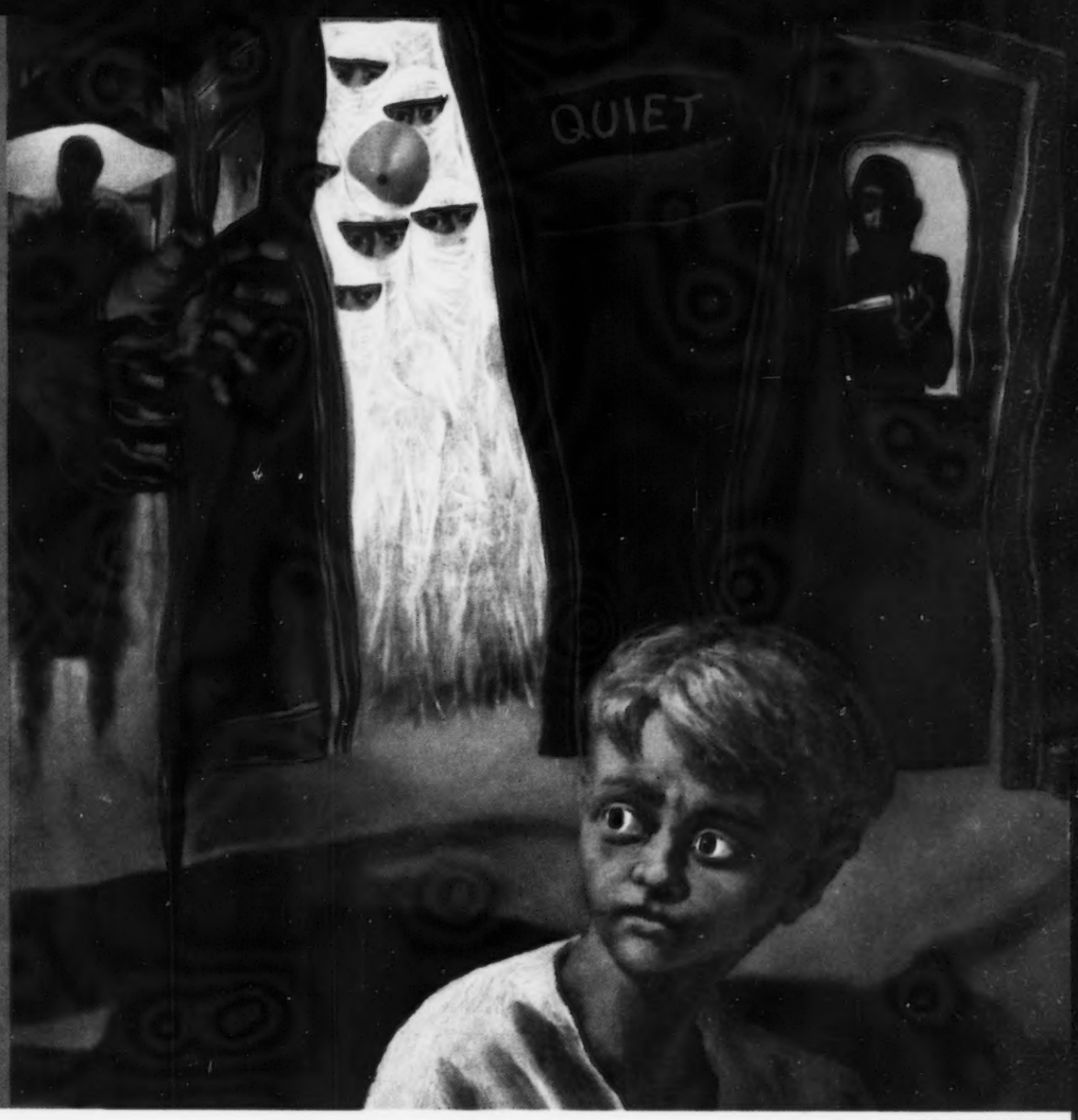
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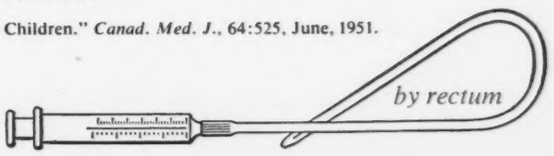
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[1]Whyte, D. W., "Special Indications for Rectal Pentothal in Children." *Canad. Med. J.*, 64:525, June, 1951.

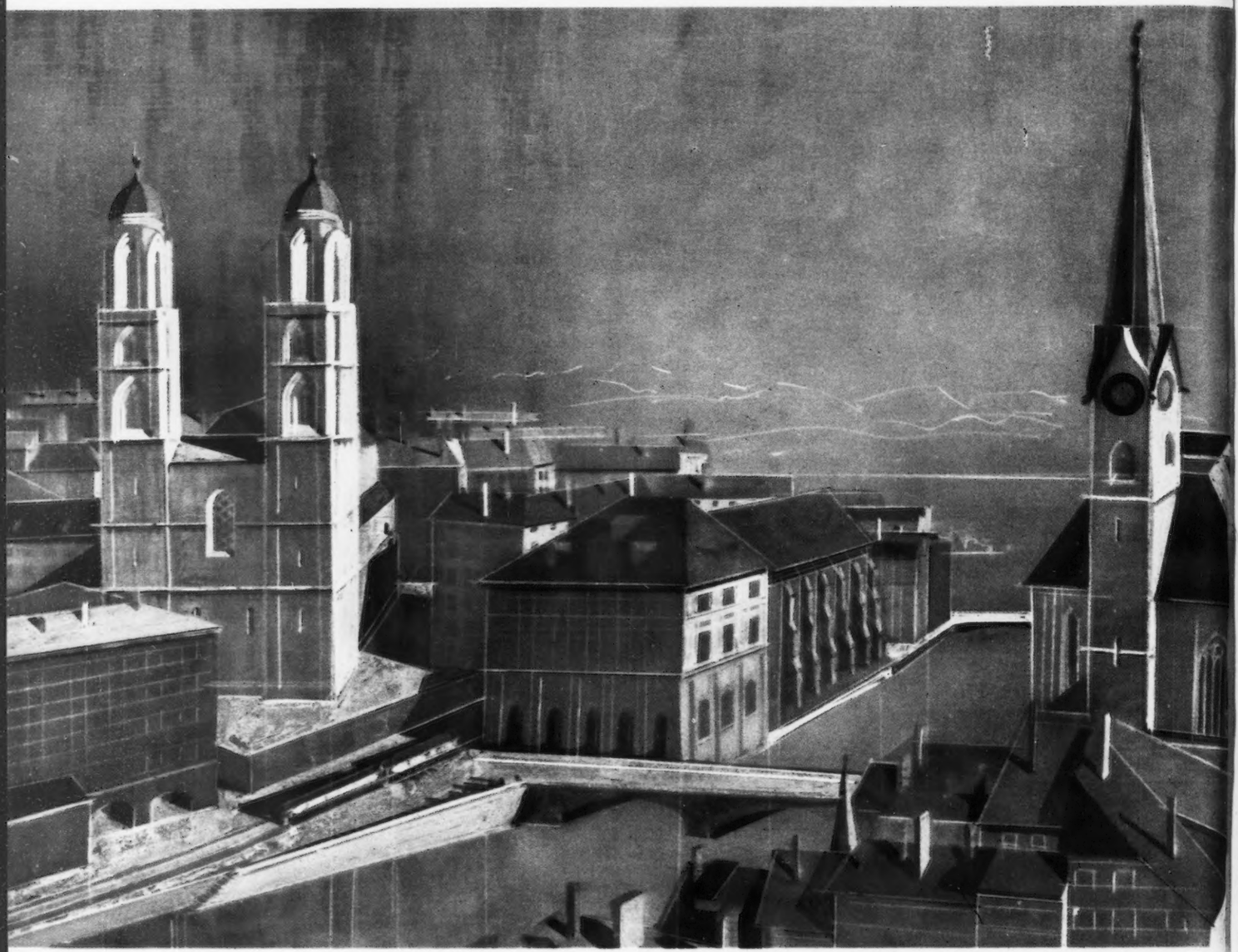
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Canad. M.A.J.
Apr. 1st, 1956, Vol. 74

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The Canadian Medical Association Journal

APRIL 1, 1956 • VOL. 74, NO. 7

METABOLIC EFFECTS OF METACORTANDRACIN (PREDNISONE) AND METACORTANDRALONE (PREDNISOLONE): COMPARISON WITH ACTH, CORTISONE, HYDROCORTISONE AND 9-ALPHA-FLUOROHYDROCORTISONE*

P. S. ROSEN,† M.D., A. J. CARTER,‡ M.D., J. A. DAUPHINEE, M.D., A. G. GORNALL, Ph.D. and M. A. OGRYZLO, M.D., *Toronto*

METACORTANDRACIN (prednisone, delta-1-cortisone) and metacortandralone (prednisolone, delta-1-hydrocortisone) are two synthetic steroids which possess glucocorticoid activity. First reports[1, 2] of their use in the treatment of rheumatoid arthritis indicated that subjective improvement may occur within six hours, objective change in the first 24 hours and continued improvement during the first week. Side-effects such as weakness, inability to concentrate, insomnia, facial rounding, hirsutism, acne and epigastric discomfort were generally of a minor degree, but in a few instances necessitated a reduction in the dose below optimum therapeutic levels. On the basis of clinical studies[3, 4] the antirheumatic activity of these new steroids has been estimated to be about four times that of cortisone or hydrocortisone. Initially little disturbance of carbohydrate metabolism was noted but later reports[3-6] have indicated that under appropriate circumstances these steroids may produce clear-cut diabetogenic effects. Salt retention was not observed. In other respects their metabolic properties were comparable to those of cortisone and hydrocortisone.

The object of the present investigation was to evaluate the therapeutic and metabolic effects of metacortandracin and metacortandralone, and to compare these with other steroid compounds including cortisone, hydrocortisone and 9-alpha-fluorohydrocortisone. All of the steroids were administered orally in divided doses; ACTH, used in one patient, was administered by intramuscular injection.

The following report deals with the observations made during the administration of these new compounds to seven patients selected from the arthritis service of Sunnybrook Hospital and carefully studied in the Clinical Investigation Unit. Five suffered from rheumatoid arthritis, one from ankylosing spondylitis and one from Reiter's syndrome. All had previously received conventional treatment including salicylates, and in some instances gold compounds, deep x-ray therapy, typhoid vaccine, phenylbutazone, cortisone or ACTH. In no case had these previous methods of therapy achieved satisfactory control of the disease.

METHODS

Careful metabolic balance studies were carried out in three patients. In the remaining four patients assessment was made on the basis of repeated determinations of the erythrocyte sedimentation rate, plasma fibrinogen, serum proteins, hæmatological changes and the degree of clinical improvement.

Plasma fibrinogen,[8] serum protein fractionation,[9, 10] sedimentation rate,[11, 12] serum cholesterol,[13] phospholipids[14] and blood sugar[15] were all followed up and determined by standard procedures, as were the urine and fæcal nitrogen,[16] urine creatine and creatinine[17] and urine

*From the Clinical Investigation Unit, Sunnybrook Hospital, and the Departments of Medicine and Pathological Chemistry, University of Toronto.

Metacortandracin (prednisone) and metacortandralone (prednisolone) were supplied as Meticorten and Meticortelone by Schering Corporation Ltd., Montreal, courtesy of Mr. F. J. Gleason. Supplies of metacortandralone (prednisolone) were also obtained from the Upjohn Company, Kalamazoo, Michigan, courtesy of Dr. C. J. O'Donovan. The 9-alpha-fluorohydrocortisone was obtained from E. R. Squibb and Sons, New Brunswick, New Jersey, courtesy of Dr. Henry Strade.

†Canadian Arthritis and Rheumatism Society Fellow in Medicine, Sunnybrook Hospital, Toronto.

‡Research Fellow, Clinical Investigation Unit, Sunnybrook Hospital, Toronto.

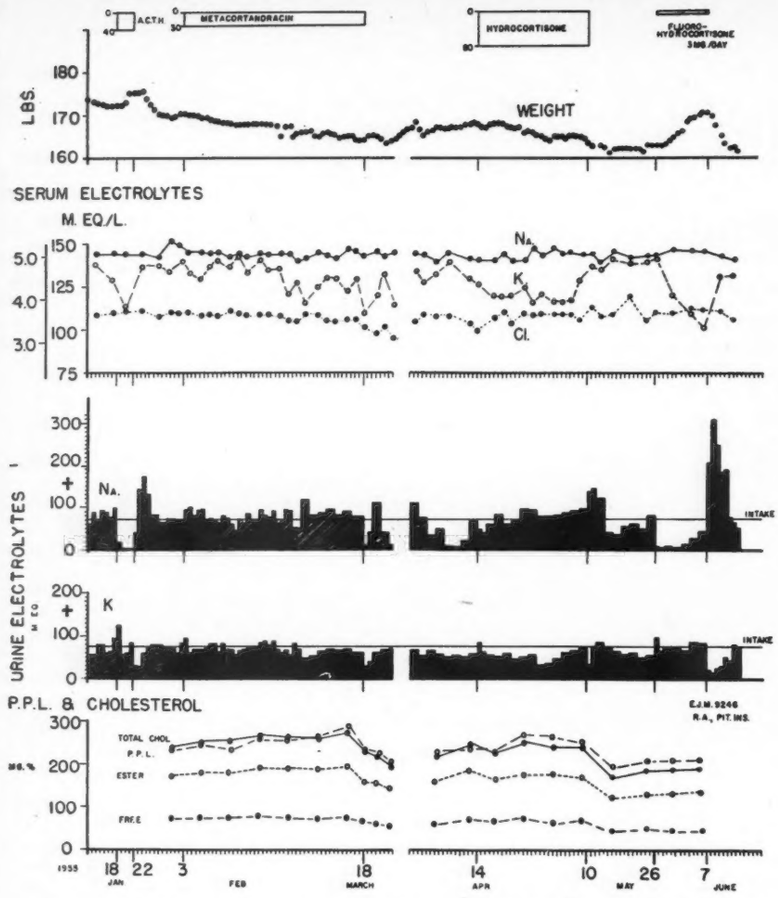


Fig. 1. (Case 1).—Pituitary tumour with pituitary insufficiency and rheumatoid arthritis; ACTH, metacortandracin, hydrocortisone and 9-alpha-fluorohydrocortisone therapy.

amino nitrogen.[18] Serum and urine electrolytes were determined for the most part by flame photometry but some values were obtained by chemical methods.[19, 20]

The 17-ketosteroid excretion was assayed by a method essentially the same as the standard procedure of the Medical Research Council of Britain.[21] Adrenal "corticoids" were determined in neutral, lipid extracts of acidified urine.[22] The normal range of "crude free corticoids" by this method is 1.5-3.0 mg. per day. When, as occurred frequently during metacortandracin administration, the urine extracts were highly pigmented, or when values above 3.0 mg. were encountered, the extracts were further purified by a benzene-water transfer. The results were then expressed as 11-oxysteroids (normal range 0.5-1.5 mg. per day).

METABOLIC BALANCE STUDIES

Balance Study No. 1. Case 1—Pituitary tumour with pituitary insufficiency and rheumatoid arthritis: ACTH, metacortandracin, hydrocortisone and 9-alpha-fluorohydrocortisone therapy.

E.J.M., a 57-year-old male, had received radiation therapy to the pituitary gland nine years previously because of an enlarged sella turcica, bitemporal hemianopia and headaches. Two years before the present admission to hospital he developed pain, stiffness and swelling of the knees and elbows, followed later by fusiform swelling of the proximal interphalangeal joints of both hands, characteristic of rheumatoid arthritis. His illness progressed despite conservative measures and immediately prior to this study his status could be described as moderately severe and active rheumatoid arthritis with multiple joint involvement (stage 2, class iii). The diagnosis of pituitary insufficiency was based on a low output of 17-ketosteroids and corticoids, with low radioactive iodine uptake and protein-bound iodine, in the presence of bitemporal hemianopia with enlargement of the sella turcica. During the study the patient was maintained on a constant diet of protein (P.), 78 g., fat (F.), 120 g., carbohydrate (CHO.), 190 g., Na. 71 mEq., K. 73.5 mEq., and a constant fluid intake to 2,000 c.c. daily.

The study consisted of: (1) a four-day test period of ACTH (Duracton*), 40 I.U. per day, (2) a control period of 14 days, (3) 42 days of metacortandracin, 30 mg. daily, (4) a control period of 29 days, (5) 26 days of hydrocortisone, 80 mg. daily, (6) a control period of 16 days, (7) eight days of 9-alpha-fluorohydrocortisone acetate, 3 mg. daily and (8) a control period of eight days. The data obtained are shown in Figs. 1, 2, and 3.

*Nordic Biochemicals Ltd. brand of long-acting ACTH.

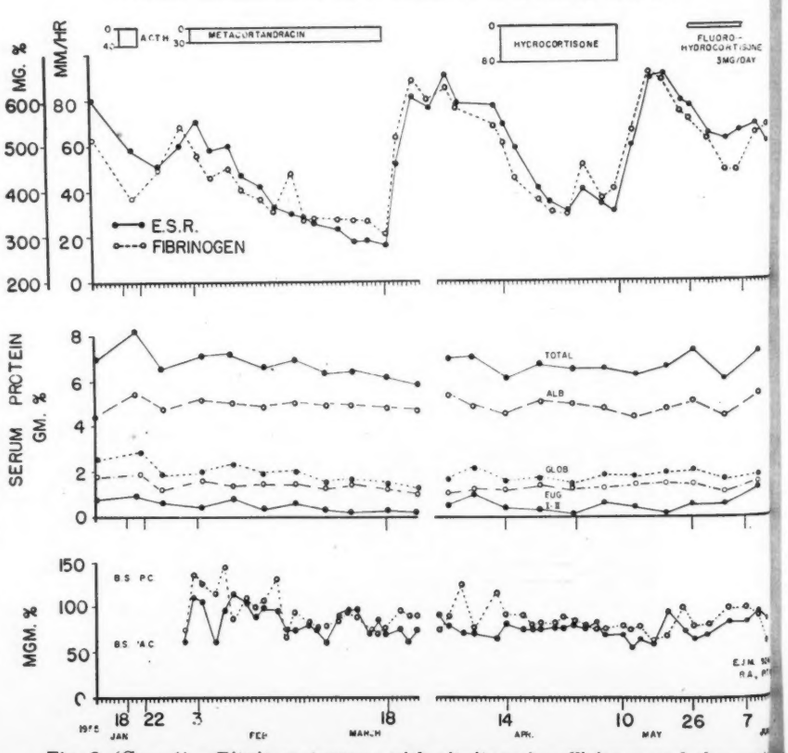


Fig. 2. (Case 1).—Pituitary tumour with pituitary insufficiency and rheumatoid arthritis; ACTH, metacortandracin, hydrocortisone and 9-alpha-fluorohydrocortisone therapy.

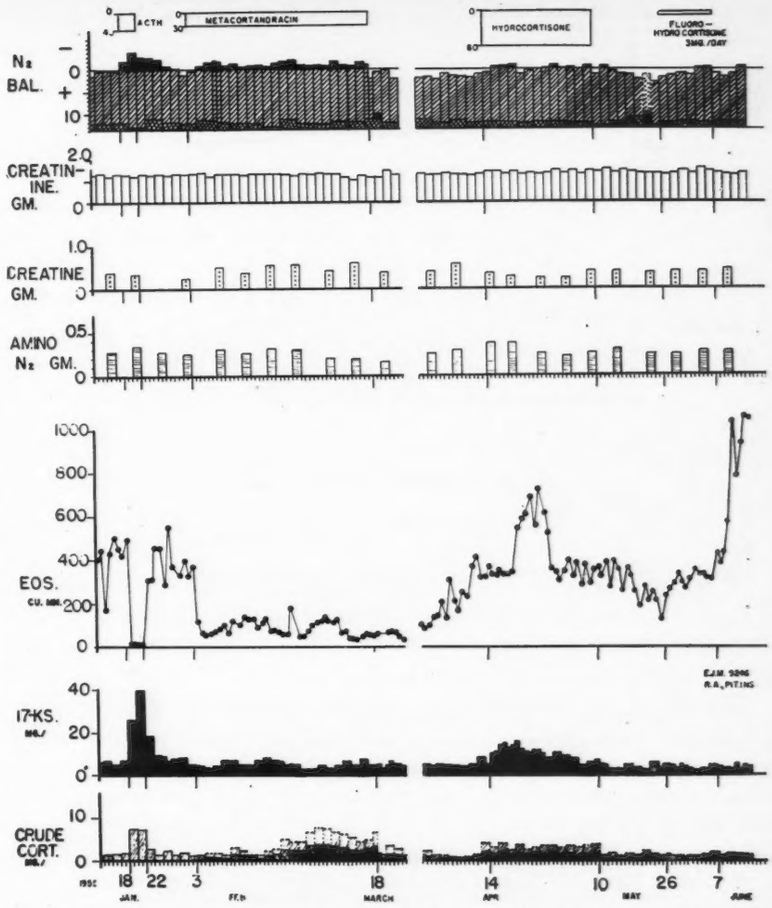


Fig. 3. (Case 1).—Pituitary tumour with pituitary insufficiency and rheumatoid arthritis; ACTH, metacortandracin, hydrocortisone and 9-alpha-fluorohydrocortisone therapy.

The administration of ACTH resulted in the following changes. The patient's weight showed an increase commencing on the second day, reaching a peak of five pounds two days after stopping injections and subsequently fell below the initial level. Marked retention of sodium, as evidenced by the low urine sodium, was noted during the period of hormone administration and was followed by a compensatory sodium diuresis. The urine potassium showed a transient increase on the first day of ACTH administration. There was a slight decrease in the serum potassium but no alteration in serum sodium or chloride. The plasma fibrinogen and erythrocyte sedimentation rate decreased slightly but returned to pre-treatment levels on termination of therapy. The serum protein fractions remained unchanged. ACTH induced a markedly negative nitrogen balance which continued for 10 days. There was a sharp drop in the circulating eosinophils to zero levels and a pronounced increase in the urinary 17-ketosteroids and corticoids during treatment, indicating a good adrenal response.

Metacortandracin administration was accompanied by a weight loss of six pounds in 42 days. There were no significant changes in serum or urine electrolytes other than a slight initial increase in the urinary sodium and potassium excretion. During the control period which followed, the patient suffered withdrawal symptoms with weakness, vomiting on one occasion, and subsequent diarrhœa. At this time the sodium balance was rather erratic and difficult to explain. Fæcal sodium values during this period were not significantly different from control periods.

Metacortandracin induced a slow but consistent drop in the sedimentation rate and plasma fibrinogen to normal levels, followed by a sharp rebound after withdrawal. A distinct negative nitrogen balance was recorded during the entire course of treatment. The eosinopenic response was only moderate in degree but this was well sustained. The urinary 17-ketosteroids remained unchanged but the corticoid values increased during the latter part of the period. During this period the corticoid assay of the urine extracts, which had become heavily pigmented, required a benzene-water transfer. The 11-oxysteroid values were free of pigment interference, and in clear extracts have been roughly half the crude corticoid values. For comparative purposes in Fig. 3, the crude corticoids are estimated to be double the 11-oxysteroid values and are plotted as broken bars above the actual 11-oxysteroid results which are cross-hatched. From chromatographic studies it was determined that the rise during therapy was due in part (15-30%) to the excretion of delta-1-cortisone and delta-1-hydrocortisone.

Hydrocortisone similarly induced a weight loss of three pounds. No significant change was noted in the serum electrolytes. The initiation of therapy was accompanied by a transient diuresis of potassium and minimal retention of sodium. Towards the end of the period the urinary sodium increased over and above the intake level and on termination there was a frank sodium diuresis. The sedimentation rate and plasma fibrinogen again decreased, but not to normal levels, and on withdrawal of the drug rebounded to their highest recorded levels. A slight negative nitrogen balance was noted, but no eosinopenia was induced. There was some increase in the urinary 17-ketosteroids and corticoids during the period.

In the subsequent control period the patient again suffered withdrawal symptoms with weakness, and vomiting on one occasion. The nitrogen content of this emesis is shown in solid

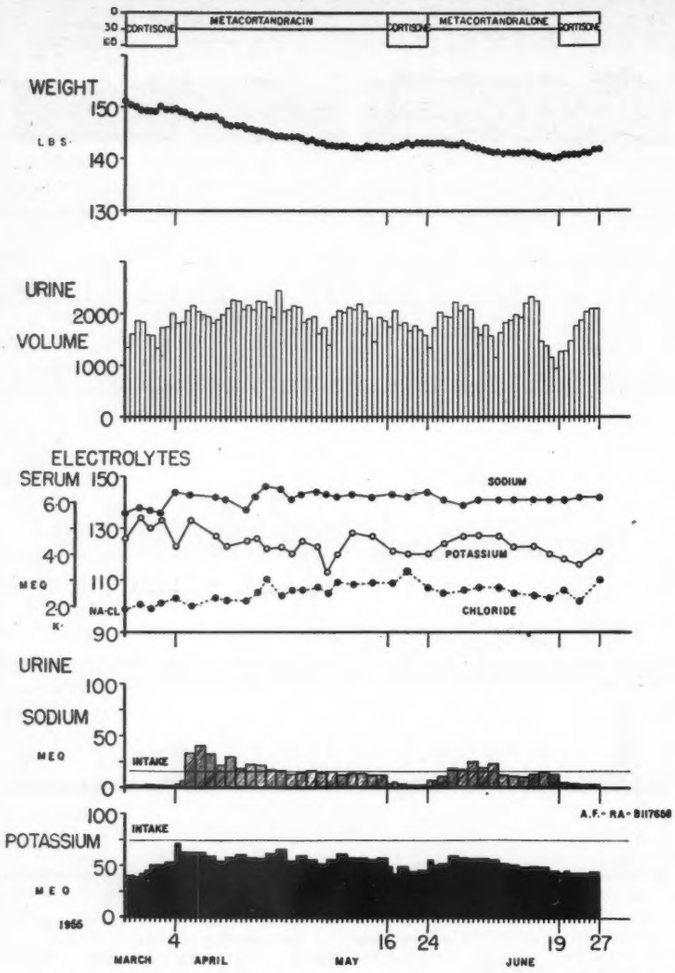


Fig. 4. (Case 2).—Rheumatoid arthritis; cortisone, metacortandracin and metacortandralone therapy.

shading in the nitrogen balance in a similar manner to the previous emesis.

With 9-alpha-fluorohydrocortisone there was a rapid weight gain of eight pounds accompanied by marked peripheral œdema. Sodium was retained in amounts comparable to or greater than that observed with ACTH, again accompanied by a transient diuresis of potassium and with a significant lowering of serum potassium. On cessation of therapy there was a marked diuresis of sodium and retention of potassium lasting for several days. The plasma fibrinogen and sedimentation rate dropped only slightly during this period, although more prolonged administration might have produced a further decline. There was no change in the nitrogen balance. The eosinophil counts remained unchanged during therapy but subsequently rose to extreme levels. No changes were noted in the 17-ketosteroids or corticoids.

Fasting and two-hour post-cibum blood-sugar levels showed little significant change throughout the whole study period. Minor changes in the total serum cholesterol, cholesterol esters and phospholipids were noted. In general these increased with steroid administration and returned to control values when the steroids were terminated. Free cholesterol remained unchanged.

Balance Study No. 2. Case 2.—Rheumatoid arthritis: cortisone, metacortandracin and metacortandralone therapy.

A.F. was a 39-year-old male with a history of multiple joint pains, stiffness and swelling of 10 years' duration. The disease had progressed to involve the hands, feet, ankles, knees, elbows, shoulders and spine, with radiological evidence of severe joint damage, and pronounced œdema with thickening of the skin of the hands and feet. There was no cardiac or renal disease. Prior to the study the condition could be classified as a severe and active rheumatoid arthritis (stage 3, class iv). Previous treatment with gold compounds, deep x-ray therapy, blood transfusion and typhoid vaccine

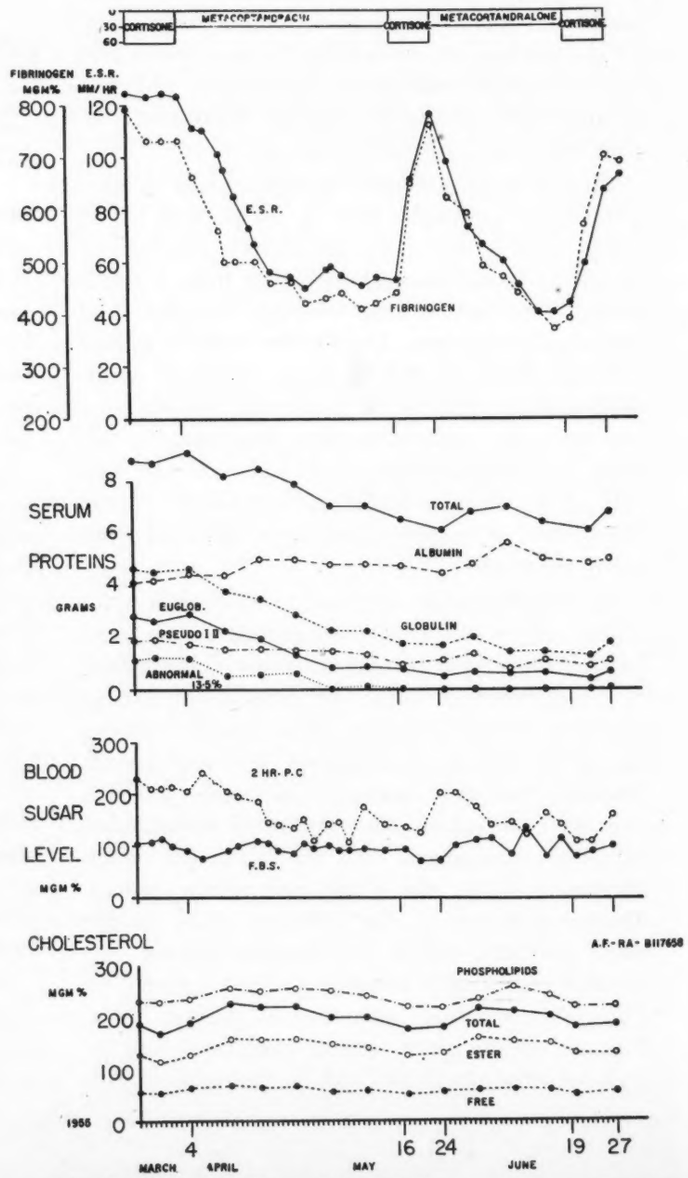


Fig. 5. (Case 2).—Rheumatoid arthritis; cortisone, metacortandracin and metacortandralone therapy.

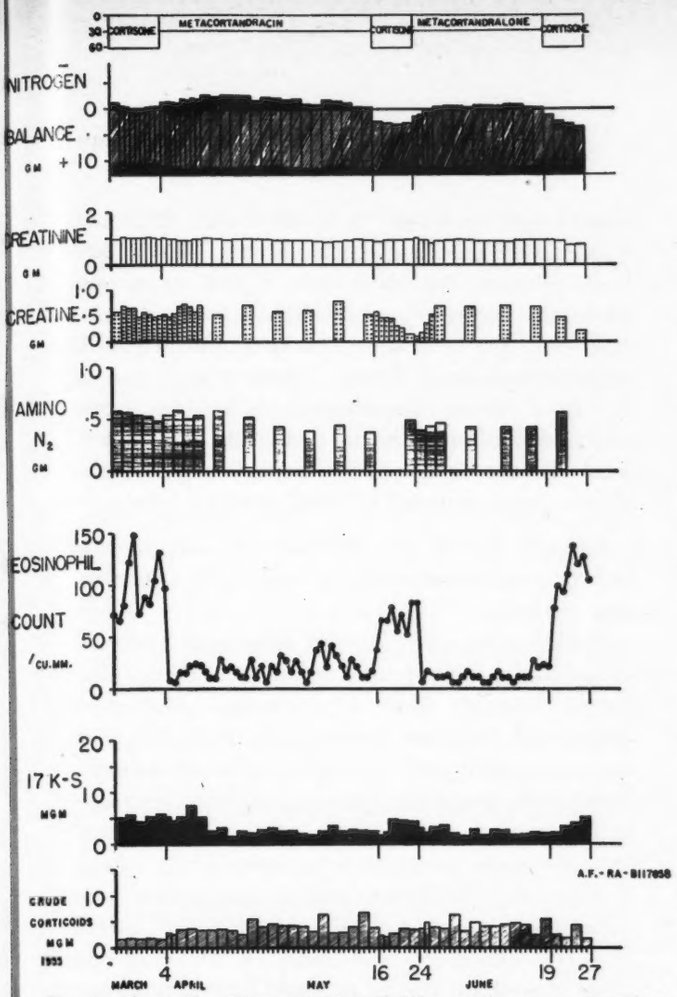


Fig. 6. (Case 2).—Rheumatoid arthritis; cortisone, metacortandracin and metacortandralone therapy.

had no influence on the course of the disease. ACTH, cortisone or hydrocortisone had been administered almost continuously for five years, with the occurrence of a number of complications including hæmatemesis, decreased carbohydrate tolerance, dependent œdema and hypertension, whenever full therapeutic doses were employed. The disease had become stabilized though not well controlled on a dose of 62.5 mg. of cortisone daily for the last four months, and rather than discontinue this therapy his status on cortisone was used for the initial control observations. Similarly the subsequent control periods represent his status on the same dose of cortisone. During the study the patient was maintained on a constant diet of P. 79 g., F. 111 g., CHO. 250 g., Na. 16.3 mEq., K. 74 mEq. and a constant intake of fluids to 2,000 c.c. daily.

The study consisted of: (1) a control period of 10 days on 62.5 mg. of cortisone daily, (2) 42 days of metacortandracin, 30 mg. daily, (3) a control period of 8 days on 62.5 mg. of cortisone daily, (4) 26 days of metacortandralone, 30 mg. daily, and (5) a control period of 8 days on 62.5 mg. of cortisone daily. The data are shown in Figs. 4, 5, and 6.

The patient's weight had remained relatively stable during the maintenance period of cortisone therapy preceding the study. During the initial control period the urinary sodium excretion averaged approximately 2 mEq. per day and the patient had peripheral œdema. The sedimentation rate and plasma fibrinogen level remained persistently elevated. The total serum proteins were 8.9 g. %, with globulin 4.8 g. % and albumin 4.1 g. %. There was some carbohydrate intolerance, with fasting blood sugar readings around 100 mg. % and two-hour postcibum blood sugar readings around 230 mg. %.

Metacortandracin administration was accompanied by a steady decline in weight totalling nine pounds, with a loss of œdema fluid and a distinct sodium diuresis which persisted for about 20 days, when sodium balance was once more established. There was a mild diuresis of potassium on the first day of therapy, and the urinary potassium values remained slightly elevated during the remainder of the period. The serum electrolytes remained unchanged.

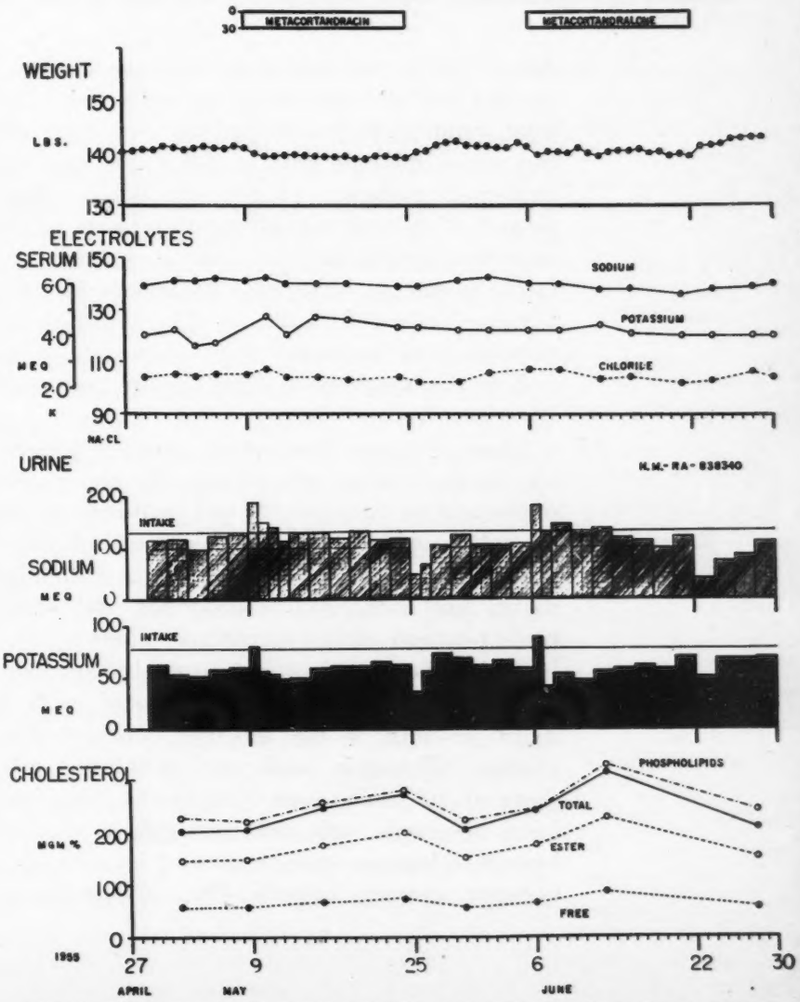


Fig. 7. (Case 3).—Rheumatoid arthritis; metacortandracin and metacortandralone therapy.

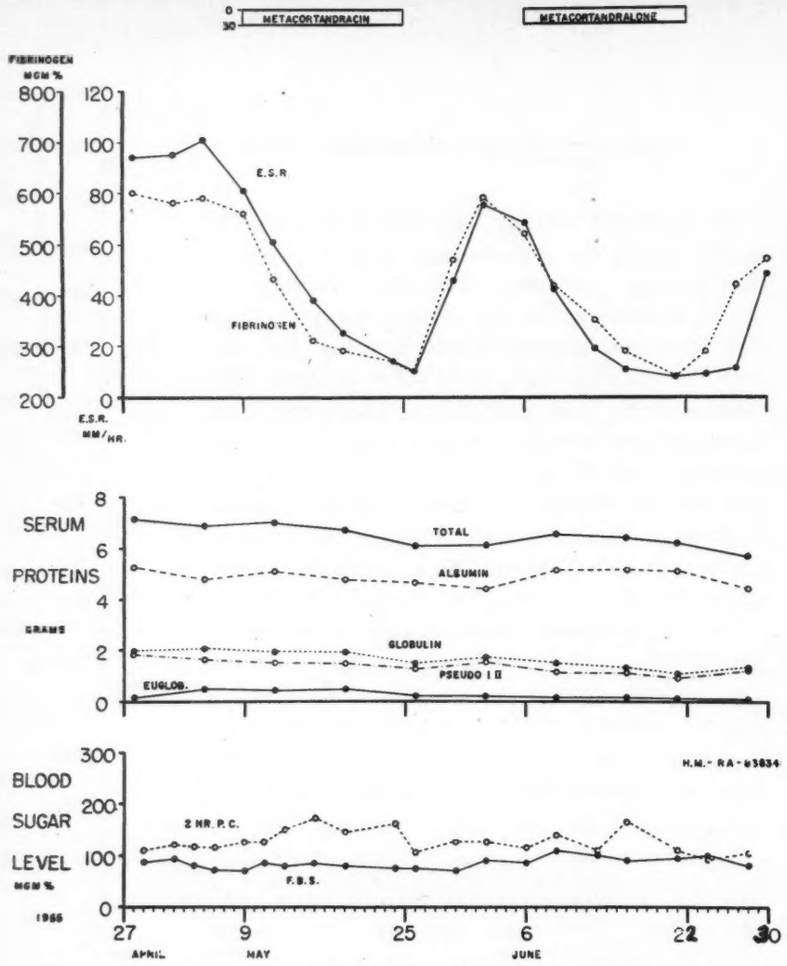


Fig. 8. (Case 3).—Rheumatoid arthritis; metacortandracin and metacortandralone therapy.

The sedimentation rate and fibrinogen level decreased but did not reach normal levels. The total serum globulin dropped to 2.3 g. % while the serum albumin rose to 4.8 g. %, and the abnormal globulin (13.5% fraction) disappeared. A marked improvement occurred in the carbohydrate tolerance, in spite of the great increase in protein breakdown as indicated by the negative nitrogen balance. The eosinopenic response was sustained and 17-ketosteroid excretion was suppressed while urinary corticoids were increased.

When cortisone therapy was resumed sodium was again retained, the plasma fibrinogen and sedimentation rate rose to pre-treatment levels as did the post-cibum blood sugar, and there was a positive nitrogen balance. The eosinophil counts and urinary 17-ketosteroids and corticoids returned almost to control values.

During the period of metacortandralone therapy, sodium diuresis was again noted, with a slight elevation in the urinary potassium. The plasma fibrinogen and sedimentation rate dropped to levels somewhat lower than had been observed with metacortandracin. Carbohydrate tolerance again improved in spite of a negative nitrogen balance. The eosinopenic response was sustained at levels lower than had been observed on metacortandracin. The urinary 17-ketosteroid excretion was again depressed while the corticoids were slightly increased.

During the periods of metacortandracin and metacortandralone therapy there was a rise in the total serum cholesterol, cholesterol esters and phospholipids, but no change in free cholesterol. In the final control period most of the observations returned to their previous levels.

Balance Study No. 3. Case 3.—Rheumatoid arthritis: metacortandracin and metacortandralone therapy.

H.McK. was a 63-year-old male with a history of multiple joint pains, stiffness and swelling dating back to 1916. The disease progressed despite all therapeutic measures, including one course of gold and a trial of phenylbutazone. Before the study the disease could be described as a severe, moderately active rheumatoid arthritis with multiple joint deformities (stage 3, class iii). During the study the patient was maintained on a constant diet of P. 79 g., F. 105 g., CHO. 206 g., Na. 130 mEq., K. 78 mEq. and a constant fluid intake to 2,000 c.c. daily.

The study consisted of: (1) a control period of 10 days, (2) 16 days of metacortandracin, 30 mg. daily, (3) a control period of 12 days, (4) 16 days of metacortandralone, 30 mg. daily, and (5) a control period of 8 days. The data obtained are shown in Figs. 7, 8, and 9.

During the administration of metacortandracin, the weight remained unchanged apart from an initial loss of one pound. There was a slight initial diuresis of sodium and potassium, with compensatory retention on withdrawal. The plasma fibrinogen and sedimentation rate dropped to normal in 16 days. There was a slight impairment of carbohydrate tolerance with the post-cibum blood sugar rising to 170 mg. %. The urinary nitrogen excretion was increased slightly during the first few days of therapy, but this was insufficient to induce a negative nitrogen balance. A good eosinopenic response was obtained. The excretion of 17-ketosteroids decreased significantly while the corticoids were increased.

During the second control period most observations returned to pre-treatment levels except for the 17-ketosteroid excretion which remained suppressed.

With metacortandralone the metabolic changes were almost identical except that there

was some suggestion that the effect on electrolytes, sedimentation rate, and the circulating eosinophils was a little more pronounced. The changes observed in the serum cholesterol and phospholipids were comparable to those in the two previous studies. No significant changes were noted in the serum proteins.

CLINICAL STUDIES

The remainder of the study includes four patients in whom balance studies were not undertaken. Evaluation of the effectiveness of the steroid compounds administered was made on the basis of careful clinical assessment together with frequent determinations of the plasma fibrinogen, sedimentation rate, hæmatological changes, eosinophil counts, weight and blood pressure readings. The data in Fig. 10 show only the fibrinogen and sedimentation rate changes, while Fig. 11 illustrates the hæmoglobin and weight changes in one undernourished, seriously ill patient.

Case 4.—J.H. was a 56-year-old male with an acute, severe rheumatoid arthritis of nine months' duration accompanied by weight loss of 35 pounds and a secondary anæmia with a hæmoglobin of 60%. He was treated first with metacortandracin over a 93-day period, followed later by metacortandralone. Metacortandracin, in a dose of 30 mg. daily, resulted in a rapid improvement in the subjective and objective manifestations of the disease, with stimulation of the appetite. The plasma fibrinogen and sedimentation rate dropped to normal after 57 days of therapy (Fig. 10a), the weight increased from 130 to 170 pounds and the hæmoglobin from 60 to 100% (Fig. 11). On reducing the daily dose to 25 mg. and later to 20 mg. daily, the plasma fibrinogen and sedimentation rate promptly rose (Fig. 10a), but did not reach pre-treatment levels. In spite of the reaccumulation of some fluid in his knees, the patient manifested no subjective exacerbation as regards joint pain or stiffness. Substitution of 20 mg. of metacortandralone at this stage resulted in a slightly greater fall in the fibrinogen and sedimentation rate over a short period. The disease has subsequently been moderately well controlled on a maintenance dose of 15 mg. of metacortandracin daily, with the sedimentation rate at about 100 mm. in one hour.

Case 5.—V.M. was a 30-year-old male with severe ankylosing spondylitis of 11 years' duration. The sedimentation rate was approximately 100 mm. in one hour and the plasma fibrinogen approximately 700 mg. %. Metacortandracin, administered in a dose of 30 mg. daily, resulted in a decrease in fibrinogen to 480 mg. % and in the sedimentation rate to 40 mm. in one hour. On withdrawal of the medication, both rose to pre-treatment levels. There was a similar response to metacortandralone in a comparable dose but the effects appeared to be somewhat more pronounced. Subjective improvement of a comparable degree was observed during both periods (Fig. 10b).

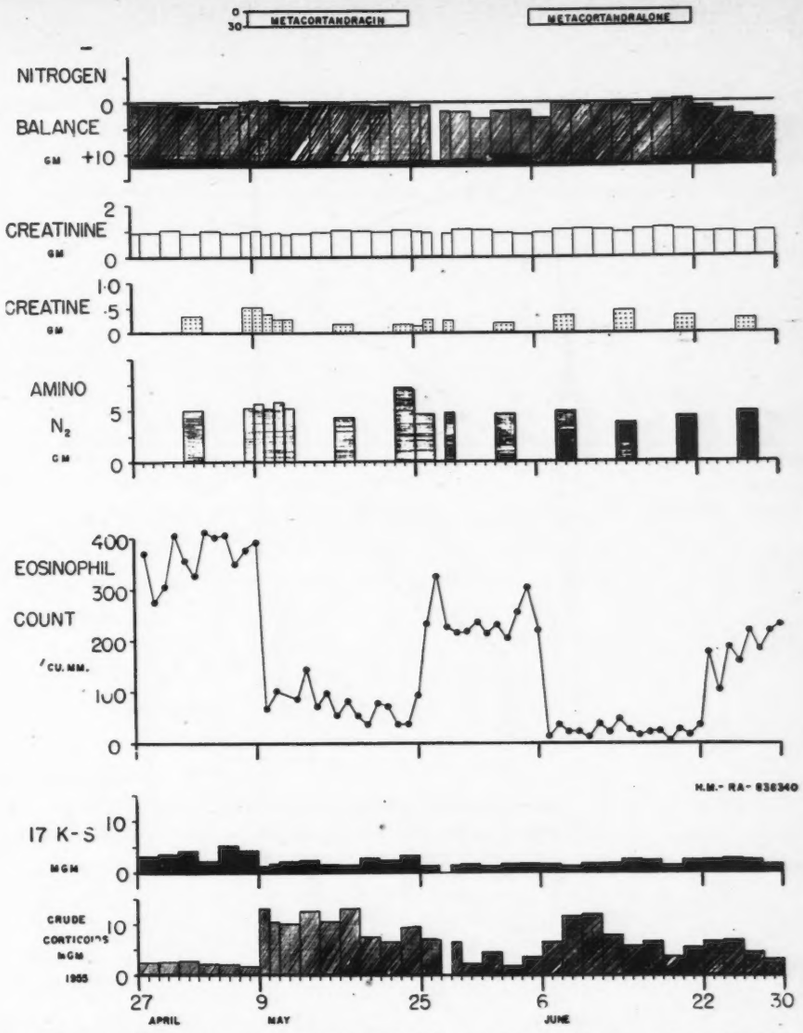


Fig. 9. (Case 3).—Rheumatoid arthritis; metacortandracin and metacortandralone therapy.

Case 6.—D.H. was a 25-year-old male with Reiter's syndrome of three months' duration. Treatment was started with 30 mg. of metacortandracin daily. Although this dose produced some subjective improvement after seven days, it was regarded as inadequate to control his symptoms. An increase to 60 mg. daily was accompanied by a greater degree of clinical improvement, with a decrease in the plasma fibrinogen and sedimentation rate almost to normal (Fig. 10c). However, several new joints later became involved, and on the suspicion

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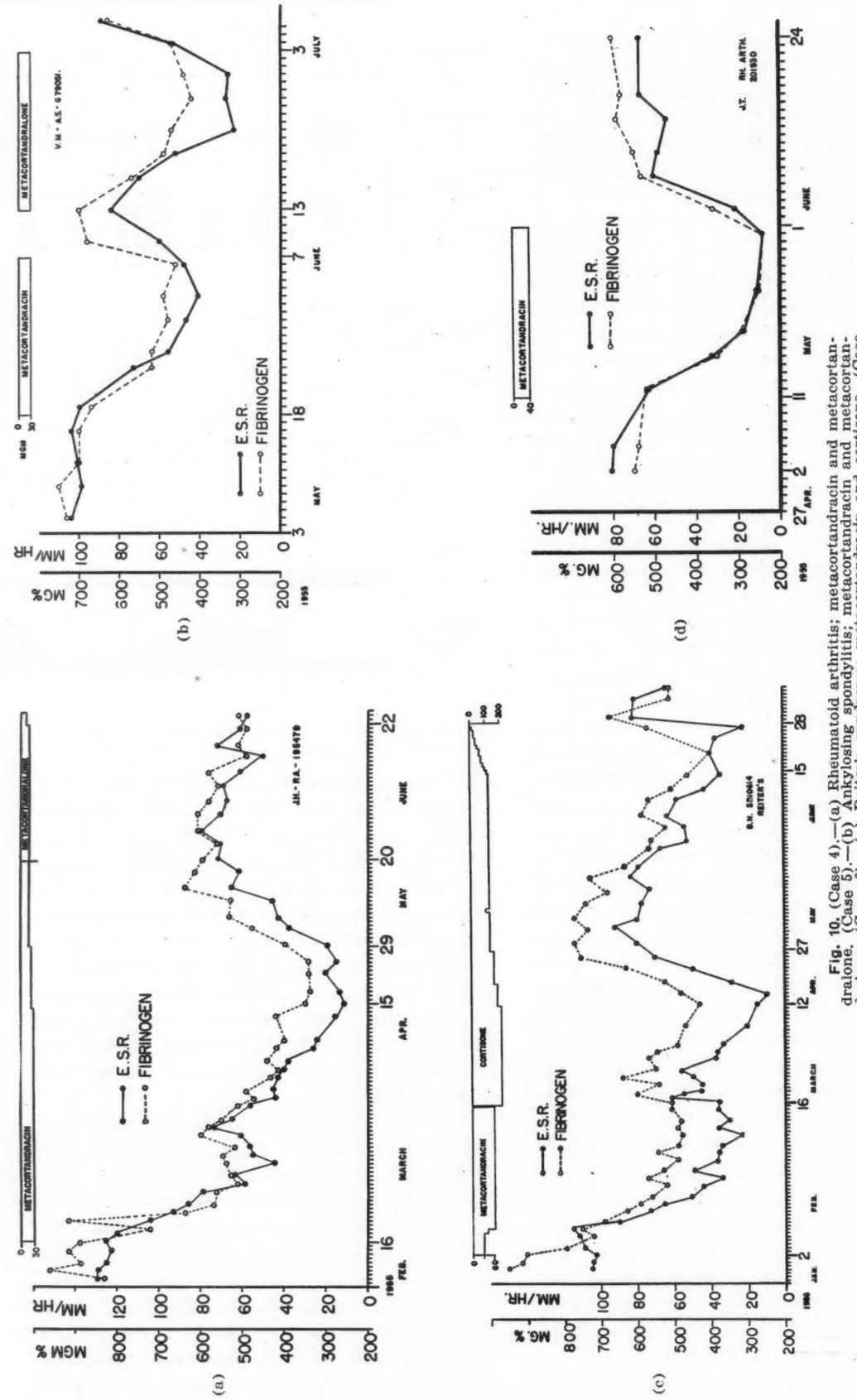


Fig. 10. (Case 4).—(a) Rheumatoid arthritis; metacortandracin and metacortandralone. (Case 5).—(b) Ankylosing spondylitis; metacortandracin and metacortandralone. (Case 6).—(c) Reiter's syndrome; metacortandracin and cortisone. (Case 7).—(d) Rheumatoid arthritis; metacortandracin therapy.

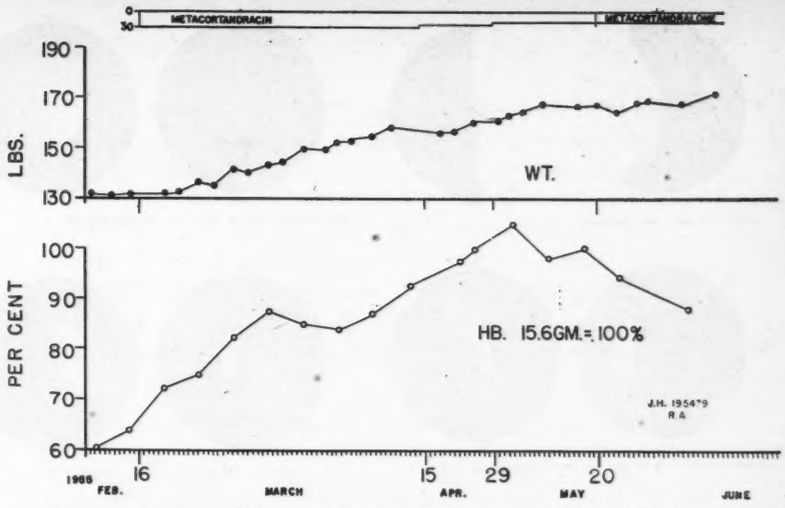


Fig. 11. (Case 4).—Rheumatoid arthritis; metacortandracin and metacortandralone therapy. Dietary intake not controlled.

that the hormonal treatment was not controlling the disease, therapy was discontinued. This withdrawal was immediately followed by a severe flare-up in all joints, with fever, excessive sweating and increased pain. Steroid therapy was promptly re-instituted, this time with cortisone in a dose of 200 mg. daily. The therapeutic effect of this dose of cortisone was equal to or somewhat better than the 60 mg. of metacortandracin, but a reduction in the dose to 150 mg. daily was followed by another exacerbation with a rise in the fibrinogen and sedimentation rate almost to pre-treatment levels. However, in spite of a reduction in the daily dose to 125 mg. later, the fibrinogen level and sedimentation rate gradually began to drop and it was felt that the patient had begun a spontaneous remission. This subsequently proved to be the case, since a further reduction in the dose by 12.5 mg. per day after June 14 was followed by only a transient mild exacerbation of his symptoms.

Case 7.—J.T. was a 59-year-old male with active rheumatoid arthritis of 30 years' duration and multiple joint deformities (stage 3, class iv). Metacortandracin, administered in a dose of 40 mg. daily for 21 days, resulted in a good clinical response and a rapid drop in the plasma fibrinogen and sedimentation rate to normal levels (Fig. 10d). Withdrawal of therapy was promptly followed by a return of these values to pre-treatment levels, although there was only a minor clinical relapse.

DISCUSSION

Anti-Inflammatory Response. — The clinical response of the inflammatory process to the administration of metacortandracin and metacortandralone in the patients studied was similar to that described in earlier reports.[1-7] All of the patients with rheumatoid arthritis and spondylitis improved rapidly during the periods of administration of these new steroids in a dose of 30 mg. per day. One patient (Case 2), poorly controlled on 62.5 mg. of cortisone per day, responded excellently to 30 mg. of metacortandracin or metacortandralone daily, and is at present maintained on a dose of 15 mg. of metacortandracin per day. In the case of Reiter's syndrome (Case 6) the disease process was not adequately suppressed by 30 mg. of metacortandracin daily, but did respond to 60 mg. per day. Withdrawal of this form of therapy was followed by a severe exacerbation and it became necessary to re-institute steroid therapy. Cortisone in a dose of 200 mg. daily controlled the clinical manifestations somewhat better than 60 mg. of metacortandracin. It is of interest that the relapse of symptoms following withdrawal of metacortandracin and metacortandralone in some patients was not as rapid or as severe as has usually been observed after cessation of cortisone therapy. There was some suggestion, on the basis of the eosinophil response and changes in the plasma fibrinogen and sedimentation rate, that 30 mg. of metacortandralone was slightly more effective than an equal dose of metacortandracin. This difference, however, was slight and may have been influenced by the order of administration.

Side-Effects.—The side-effects produced by these drugs were similar to those reported by others and have already been mentioned. The patient with the pituitary tumour and bitemporal hemianopia (Case 1) was subsequently shown at operation to have a cystic craniopharyngioma. During the course of metacortandracin therapy, there occurred a marked reduction in visual fields (Fig. 12). The severity of this change necessitated a break in the study in order to undertake further investigations. Within a short period the visual fields returned nearly to pre-treatment configuration and the study was continued. The administration of hydrocortisone was likewise accompanied by a decrease in the size of the visual fields, but this time withdrawal of the hormone was not followed by the same degree of improvement. A similar occurrence was noted with fluorohydrocortisone therapy. It was this unfavourable response which prompted the exploration of the pituitary fossa.

Withdrawal Symptoms. — Severe withdrawal symptoms occurred on two occasions in one patient (Case 1), three days after cessation of

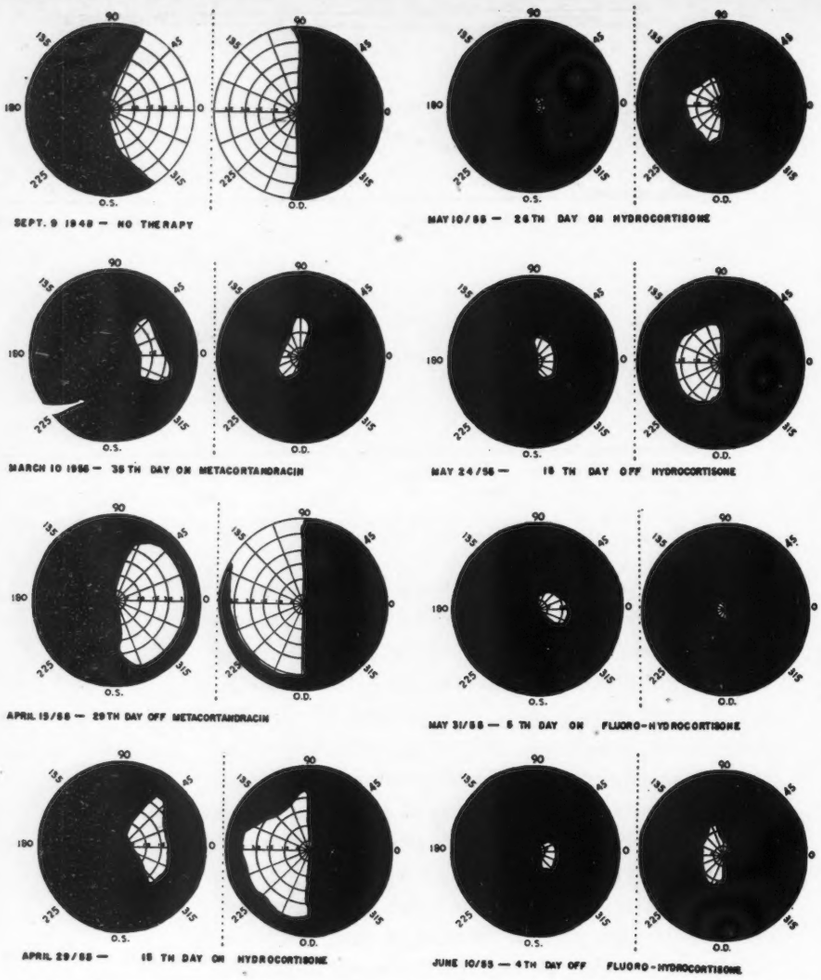


Fig. 12. (Case 1).—Pituitary tumour with pituitary insufficiency and rheumatoid arthritis; visual field changes while receiving steroid therapy.

metacortandracin therapy and three days after cessation of hydrocortisone therapy. These were characterized by weakness, headache, nausea, vomiting, diarrhœa, shortness of breath and bronchospasm. During these periods the patient also developed, for the first time, typical attacks of severe biliary colic. A flat plate of the abdomen revealed a calcified, radio-opaque gallbladder, indicating chronic gallbladder disease. One other patient had mild diarrhœa (Case 3).

METABOLIC ACTIVITY OF METACORTANDRACIN AND METACORTANDRALONE

Metacortandracin and metacortandralone have been observed to produce similar metabolic effects. The administration of these steroids resulted in an increase in urinary nitrogen excretion on a controlled dietary intake, with a concomitant loss of weight. Only minor alterations in serum electrolytes were noted. There was usually a mild sodium and potassium diuresis on the initiation of therapy, with compensatory retention on withdrawal. There was no evidence of sodium retention.

Elevation of the serum albumin with a depression of the total globulin and the abnormal globulin (13.5% fraction) was noted in one patient (Case 2). This patient had markedly elevated serum globulins and depressed albumin before the study.

Both steroids produced a prompt decline in the plasma fibrinogen and sedimentation rate. The fibrinogen levels often gave an earlier indication of change in activity and a more accurate picture of the severity of an exacerbation than did the sedimentation rate, but for the most part they followed a parallel course.

A slight decrease in the carbohydrate tolerance was noted in one patient as indicated by the increase in post-cibum blood sugar levels (Case 3). Improvement in carbohydrate tolerance was noted in one other patient (Case 2) who had previously been receiving cortisone therapy. This occurred in spite of evidence of increased protein breakdown.

Metacortandracin and metacortandralone administration produced a prompt and uniform decrease in the number of circulating eosinophils. In two patients suppression of urinary 17-ketosteroids was noted. In the patient with hypopituitarism, no suppression was noted. Urinary corticoid levels rose to a notable extent during the administration of these steroids.

Frequent determinations of the serum uric acid prior to and during the studies revealed no consistent changes. Daily determinations of blood pressure revealed no tendency to develop hypertension. Changes in the electrocardiograms were noted in most patients during the administration of these hormones. These consisted principally of alterations in the configuration of the T waves, but could not be related to changes in the level of serum potassium.

COMPARISON WITH CORTISONE, HYDROCORTISONE AND FLUOROHYDROCORTISONE

Metacortandracin and metacortandralone have anti-inflammatory properties qualitatively similar to those of cortisone and hydrocortisone, as indicated by their effect on the clinical course of the disease in patients with inflammatory joint disease, as well as on the plasma fibrinogen and sedimentation rate. Weight for weight they appear to be approximately three times as effective as cortisone or hydrocortisone. The increased excretion of free corticoids during the administration of these steroids suggests that their greater effectiveness may be due to a longer biological half life. They have the further

advantage of lacking any tendency to cause sodium and water retention when administered in therapeutic doses. A somewhat greater rate of nitrogen excretion was induced with a dose of 30 mg. daily than is usually observed with comparable therapeutic doses of cortisone or hydrocortisone when a constant intake of protein and calories was maintained, suggesting that this dose is unsuitable for prolonged administration. However, when a liberal intake of protein and calories is permitted in undernourished patients, one may sometimes observe a dramatic improvement with a rapid gain in weight and a rise in the hæmoglobin level (Fig. 11). The present studies would indicate that metacortandracin and metacortandralone can influence carbohydrate metabolism, although this may not be as marked as with cortisone or hydrocortisone. The sustained suppression of the circulating eosinophils after withdrawal of the hormone in one patient suggests that they may have some cumulative effect. The urinary 17-ketosteroid excretion tended to be suppressed to a greater degree than with cortisone or hydrocortisone.

Fluorohydrocortisone was also observed to have anti-inflammatory action, but the marked salt-retaining properties of this hormone make it an unsuitable agent for this purpose.[23]

SUMMARY

Metacortandracin and metacortandralone are two synthetic steroids possessing enhanced anti-inflammatory properties. The administration of these compounds to five patients with rheumatoid arthritis, one patient with ankylosing spondylitis and one patient with Reiter's syndrome was followed by a prompt suppression of joint manifestations and an increased sense of well-being, and was accompanied by a drop in the sedimentation rate and level of plasma fibrinogen in all instances. Their antirheumatic activity appeared to be at least three times that of cortisone or hydrocortisone. Undesirable side-effects were observed in some of the patients, but these were not severe and could be minimized by a reduction in the dose within the range of therapeutic effectiveness.

With a dose of 30 mg. daily and a fixed dietary intake, these steroids exhibited no sodium-retaining properties and were sometimes accompanied by a distinct diuresis of sodium. They produced a greater negative nitrogen balance than comparable antirheumatic doses of cortisone or hydrocortisone. The effect on carbohydrate metabolism tended to be less marked, while adrenal cortical suppression was greater than that observed with cortisone or hydrocortisone. In other respects their metabolic effects were similar to those of other steroids with glucocorticoid activity.

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RÉSUMÉ

La métacortandracine et la métacortandralone sont deux stéroïdes synthétiques possédant des propriétés anti-inflammatoires élevées. L'administration de ces composés à 5 malades souffrant d'arthrite rhumatoïde, à un malade souffrant de spondylose ankylosante, et à un malade présentant le syndrome de Reiter fut suivie par une rapide disparition des signes articulaires et un bien-être accru, et fut accompagnée par une baisse du taux de sédimentation et du niveau de fibrinogène plasmatique, dans tous les cas. L'activité anti-rhumatismale de ces composés semble être au moins 3 fois celle de la cortisone ou de l'hydrocortisone. Chez quelques malades, on observa des effets secondaires désagréables mais non sérieux et qui pouvaient être diminués par une réduction de la dose n'affectant pas son efficacité thérapeutique.

Avec une dose quotidienne de 30 mg. et un régime déchloruré bien déterminé, ces stéroïdes ne causèrent aucune rétention sodique; leur administration fut quelquefois accompagné par une diurèse distincte de sodium. Ils produisirent un équilibre azotique négatif plus marqué que des doses anti-rhumatismales comparables de cortisone ou d'hydrocortisone. L'effet sur le métabolisme des hydrates de carbone sembla moins prononcé, tandis que l'effet de la suppression cortico-surrénalienne dépassait celle qu'on observe avec la cortisone ou l'hydrocortisone. En d'autres domaines, leurs effets métaboliques furent semblables à ceux d'autres stéroïdes à activité glucocorticoïde.

M.R.D.

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SURGICAL PROCEDURES OF VALUE IN RHEUMATOID ARTHRITIS*

W. ROBERT HARRIS, M.D., F.R.C.S.[C.],
Toronto

THE ASSESSMENT of surgical procedures in the treatment of rheumatoid arthritis is always complicated by the special problems attending each patient, as well as by the fact that most surgeons are reluctant to advise very radical procedures for such a seemingly hopeless disease. Nevertheless, it has become apparent that certain procedures are of definite value, and that they can be offered to sufferers fairly early in the course of their illness with some certainty of improvement.

To clarify the situation, this paper reviews the experience on the Orthopædic Service of the Toronto General Hospital during the past five years. In all, 54 operations were performed on 34 patients. These are listed in Table I, together with their results, and the ensuing text discusses the indications for and limitations of the procedures in more detail.

RESULTS

Surgery and the Activity of the Disease.—The relationship of surgery to the activity of the disease remains an open question. Opinions vary from that of Smith-Petersen,[1] who felt that successful treatment of one joint removed a source of pain and toxicity and so produced a general improvement in the disease, to the more widely held view that surgery may precipitate an acute generalized flare-up. The observed facts in this series do not lend support to either concept. Half (18 of 34) were operated upon while the sedimentation rate was grossly elevated. In none of these was there evidence to suggest that the disease was either improved or aggravated by the surgery. Of the remainder, who were operated upon while the disease was quiescent (as judged by the sedimentation rate), none had an obvious flare-up of the disease. It seems fair to conclude from this that surgery does not alter the progress of the disease in any way. As a general principle, however, it is wise to withhold surgery until the disease is relatively quiescent, as the prognosis can then be determined more accurately.

The Use of Steroid Hormones with Surgery.—Cortisone or ACTH has been used in conjunction with surgery in nine patients in this series. Seven received the drugs during the postoperative period, and two were given treatment both before and after surgery. The doses used were somewhat empirical and varied with individual patients, but in the main were the amounts used in the ordinary therapy of rheumatoid arthritis. The duration of treatment varied widely, ranging from two to three weeks in most to two years in two patients who are still receiving the drugs. There is no question but that the use of these drugs has greatly facilitated the postoperative management by reducing and allowing earlier and more successful physiotherapy. There was nothing to suggest that the hormones interfered with wound healing, or that they increased the incidence of postoperative infection.

Arthroplasties.—Arthroplasties of two kinds were employed in the series. In the first of these, the excision arthroplasty, the bone ends are excised in the hope of establishing a fibrous ankylosis. In the second, the replacement arthroplasty, one joint surface is excised and replaced by an inert material or prosthesis, which resembles as nearly as possible in size and shape the normal articular surface. Excision arthroplasties were performed 16 times: temporo-mandibular joint 2, elbow 7, hips 4, knee 2, toes 1. Our experience has been that, although this form of arthroplasty results in a satisfactory increase in the range of movement, it does so at the expense of producing a flail joint. This is so unstable as to be quite unsatisfactory in a weight-bearing limb. Thus, of the two patients who had bilateral excision arthroplasty of the hip, one has had an unsatisfactory result, while the other is improved mainly because the operation allows him comfortable sitting whereas he was bed-fast before. In the elbow and temporo-mandibular joints, where instability is a lesser consequence, the results have been very satisfactory and have been of benefit to the patients in allowing them to feed and care for themselves again. The one failure in this group was with an elbow arthroplasty which went on to bony ankylosis despite vigorous physiotherapy and cortisone. This unhappy tendency of excision operations to heal by bone rather than fibrous tissue is fortunately not common. Various interpositioning materials

*From the Division of Orthopædic Surgery, Toronto General Hospital. Read before the annual meeting of the Canadian Rheumatism Association, Toronto, June 1955.

such as fascia, nylon, and vitallium moulds are used to combat this. These assist in the formation of a new joint, but of course do not contribute to its stability. It is our view that early movement after surgery is the important essential, and that the use of cortisone postoperatively greatly facilitates this. The only exception to the rule of avoiding excision arthroplasties in weightbearing joints is in the case of the metatarsophalangeal joints. In the stiff, deformed forefoot, removal of protruding metatarsal heads eliminates a source of painful callosities, and allows comfortable walking. Although our experience is limited to one case, the result is so satisfactory that we feel this operation should be offered more frequently.

The group of replacement arthroplasties was confined to the hip, which because of its mechanical arrangement is particularly suitable for this kind of operation. We have found that a metal prosthesis with a curved stem fitting into the femoral shaft is much more satisfactory than the original plastic device described by Judet. This operation has been performed 16 times. Two patients, both with bilateral operations, went on to bony ankylosis and are counted as failures. A third developed wound infection and is also a failure. All of the remainder have been improved—some spectacularly. The most significant improvement has been relief of pain. Movement has not been increased in every case, but in most the range has been improved, or, what is equally important, the arc of movement has been altered so that a troublesome flexion deformity has been eliminated. In a few cases, at first much improved, there has been an increasing loss of function with the passage of time. This appears to be due to osteoporosis of the adjacent bone, so that the position of the prosthesis has altered. We feel that the chances of success in hip arthroplasty are increased if there is sclerosis of bone about the joint at the time of operation.

Arthrodesis.—Although deliberate fusion of a joint in rheumatoid arthritis may seem to be a contrary aim, this procedure remains the most effective means at our disposal for the control of pain. Thus in those joints so badly destroyed by the disease that they have little movement but considerable pain, arthrodesis offers definite improvement. In addition, it can be used to correct deformity. We have used arthrodesis only in the weightbearing joints, and have performed it in six knees and three feet. The results have been most satisfactory in each case; indeed two patients who had been bedridden for years were successfully rehabilitated after knee arthrodesis. It goes without saying that the procedure should be confined to those patients who have single major-joint involvement: the combination of a stiff hip and a stiff knee in the same limb is particularly disabling.

TABLE I.

	No. of procedures	*Result*	
		Improvement	*Failure*
Arthroplasty			
Jaw	2	2	0
Elbow	7	6	1
Hip	20	15	5
Knee	2	0	2
Toes	1	1	0
Arthrodesis			
Knee	6	6	0
Foot	3	3	0
Capsulotomy			
Hip	3	3	0
Osteotomy			
Knee	3	3	0
Synovectomy			
Knee	7	6	1

Tenotomy and Capsulotomy.—Persistent muscle spasm is a major deforming factor in rheumatoid arthritis, and if untreated leads to fixed flexion deformities due to fibrosis of the adjacent soft tissues. Most of these problems respond to repeated application of plaster. If this method fails, and if joint destruction is minimal (i.e. the joint retains a reasonable range of movement in flexion), then soft tissue must be divided surgically. All fibrotic tissues, including the joint capsule if necessary, should be divided. This type of operation has been done on three hips, and in each case resulted in considerable improvement in that the patients could stand more erect, and were freed of the troublesome hyperlordosis of their lumbar spines. It is of interest that each patient remarked on the disappearance of the feeling of tightness in the joint formerly experienced on attempting to stand up.

Although no knees have been operated upon in this series, it is our feeling that this operation should be done more frequently, and earlier than is commonly supposed. This is for two reasons: (1) untreated flexion deformity at the knee causes a secondary flexion deformity of the hip, and (2) contracture in the hamstrings is such that attempts to correct it by plasters alone lead to posterior dislocation of the knee, a defor-

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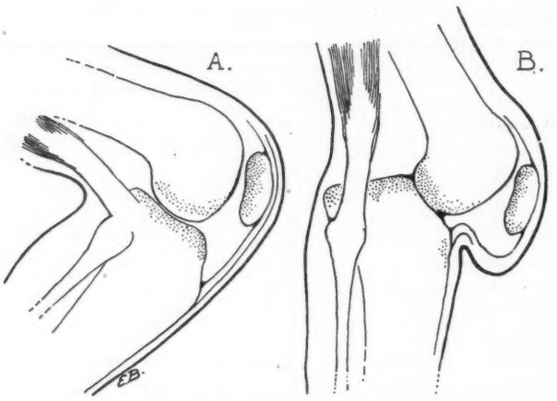


Fig. 1.—To show that attempted correction of a knee flexion deformity, when due to contracture of the hamstrings, leads to posterior dislocation of the tibia.

mity quite as troublesome as the original one (Fig. 1).

Osteotomy.—Flexion deformities of long standing may prove resistant even to capsulotomy; such cases can be corrected by division of the bone adjacent to the joint. The indications are the same as for capsulotomy, namely, a joint which cannot be completely extended but which retains a useful range of movement in flexion. Supracondylar osteotomy of the femur has been performed three times in this series with satisfactory improvement in each case (Fig. 2).

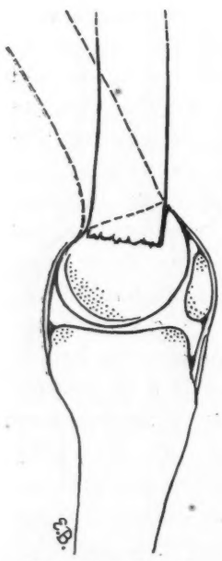


Fig. 2. — To show correction of a knee flexion deformity by osteotomy of the femur in the supra-condylar area.

Synovectomy.—Synovectomy of the knee joint has fallen into disrepute in recent years. Nevertheless, one occasionally encounters a chronic hydrops of the knee, resistant to conservative measures including hydrocortisone (compound F) administration, in which the joint retains a good range of movement and in which the radiographs show minimal bony destruction. These cases are definitely improved by synovectomy, which reduces the amount of fluid and provides a much more comfortable joint. We have performed seven synovectomies in four patients. All but one have been improved. It is of interest that the one failure occurred in the pre-cortisone era; this patient subsequently had his other knee operated upon, and has an extremely good result, presumably due to the postoperative use of cortisone.

SUMMARY

Although this group of cases is too small to permit accurate statistical analysis, certain general findings have come to light which are worth recording.

1. Surgical procedures do not affect the course of this systemic illness in any particular way. However, surgery should be withheld until the disease is relatively quiescent, as the prognosis can then be more accurately determined.

2. Arthroplasty by the excision method is almost certain to produce increased movement. The instability produced is so great as to make it of little value in weightbearing joints. In these, some form of replacement arthroplasty is required.

3. Arthrodesis remains the most effective method of reducing pain, and is the most useful procedure in weightbearing joints which have little movement and much pain.

4. Division of soft tissue or bone for the release of flexion contracture is of definite value in those joints which retain a range of movement in flexion, and should probably be performed rather earlier than is customary, particularly in the knee joint.

RÉSUMÉ

L'auteur rapporte certains faits d'ordre général découverts grâce à l'étude d'un groupe de cas malheureusement pas assez nombreux pour permettre une analyse statistique exacte.

Les modes opératoires n'ont pas d'influence particulière sur les cours de cette maladie systémique (l'arthrite rhumatoïde). Cependant, on doit s'abstenir de toute intervention chirurgicale pendant les périodes d'activité de la maladie. Dans ce cas, le pronostic peut être déterminé avec plus de précision.

L'arthroplasie, par la méthode de l'excision, procure presque toujours une plus grande mobilité. L'instabilité obtenue est si grande qu'elle n'est pas recommandable pour les articulations qui doivent supporter un poids. Pour ces dernières, une arthroplasie de remplacement est nécessaire.

L'arthrodèse (opération d'Albert) demeure la méthode la plus efficace pour diminuer la douleur et constitue le mode opératoire le plus utile pour les articulations supportant un poids, qui ont un mouvement très diminué et sont le siège de beaucoup de douleur.

La division des tissus mous ou de l'os pour le relâchement de la contracture de flexion est d'une valeur bien établie dans les cas d'articulations qui conservent une certaine portée de mouvement dans la flexion. Elle devrait probablement être pratiquée plus tôt qu'il n'est d'usage, surtout dans l'articulation du genou. M.R.D.

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ASSESSMENT OF THERAPEUTIC AGENTS IN RHEUMATOID ARTHRITIS*

LESLIE MANDEL, M.D., M.R.C.P.(Lond.),
Ottawa, Ont.

CAREFULLY CONTROLLED experimental methods for the evaluation of new therapeutic agents are essential in all therapeutic trials, whatever be the disease treated. "Therapeutics," said Professor Pickering in 1949, in his presidential address to the section of Experimental Medicine and Therapeutics of the Royal Society of Medicine,[1] "is the branch of medicine that, by its very nature, should be experimental."

Scientific experimental methods of assessment are particularly applicable to such a capricious disease as rheumatoid arthritis where the clinical course, pattern and natural history are so variable as to be unpredictable in any particular patient. The disease runs a naturally fluctuant course with spontaneous remissions and exacerbations of variable duration. Quite apart from the normal fluctuations which occur as part of the natural history of the disease, the psychological effect of giving a new treatment may be considerable. Psychological factors may not only influence the patient's symptoms and mental attitude, but also lead to personal bias on the part of an enthusiastic observer anxious to demonstrate his pet idea.

Failure to appreciate these facts has been largely responsible for unsatisfactory and uncontrolled methods of assessing the efficacy of therapeutic agents in rheumatoid arthritis. That many therapeutic trials have been carried out with unsatisfactory experimental methods is shown by the marked discrepancies that have been reported with the same agent under investigation. This is particularly illustrated by the recent use of deoxycortone combined with ascorbic acid; several workers claimed good results[2-15] and others were more sceptical.[16-28] Therapeutic results claimed with uncontrolled work are likely to be fallacious, and yet are often quoted and requoted and may finally be unequivocally accepted. This is regrettable, particularly if such reports are given widespread publicity both in the medical and lay press, and exploited by commercial interests.

*Paper read at a Scientific Session of the Canadian Rheumatism Association in June 1955. Extracted from a thesis accepted for the degree of M.D., University of Liverpool, 1953.

In addition to lack of controls, in many therapeutic reports there is an absence of satisfactory standard criteria for evaluating and grading results. This makes any comparison of such results almost impossible. Another source of confusion in several reports is the failure to distinguish between the effects of therapy on rheumatoid activity in contradistinction to its influence on functional capacity. These difficulties, together with discrepancies of results due to uncontrolled methods, are probably the chief reasons for the multitude of therapeutic agents that have been and still are being used for the treatment of rheumatoid arthritis.

In view of the unsatisfactory state of affairs in appraising the results of therapy, an attempt has been made to find suitably controlled methods of assessment which would show whether or not a beneficial effect was due to an agent under trial. The degree of association between the methods has been determined by the calculation of correlation coefficients. The methods have also been analyzed to ascertain which of them are most suitable for agents acting slowly, agents acting rapidly, and agents applied to a joint to produce a local effect. In addition, the various ways of employing controls have been given careful consideration.

PREVIOUS WORK AND OBSERVATIONS

In 1937, in the presidential address at the Fourth Annual Meeting of the American Rheumatism Association, Cecil[29] made a plea for the appointment of a committee to set up certain criteria for the diagnosis and cure of rheumatoid arthritis. The deficiency of adequate criteria was emphasized in 1946 by Steinbrocker,[30] as the outcome of attempting to correlate the results of gold therapy in his clinic with those of other workers. He recommended certain safeguards in order to ensure accurate and reliable evaluation of therapy.

In the same year, Steinbrocker and Blazer[31] published a standardized method of appraising the results of therapy, using what was described as a "therapeutic score card". The principle of the system was to employ the chief features of rheumatoid arthritis and to assign percentage values to each of them, so that exact calculations and comparisons could be made. Previously, in 1943, Bayles and Hall[32] planned a chart that could be used as a yardstick for the treatment of rheumatoid arthritis.

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Tegner,[33] in the presidential address to the Section of Physical Medicine of the Royal Society of Medicine, also drew attention to the difficulty in appraising the results of treatment. He placed his patients into three categories of improvement. These were used and modified by Ney[34] in a report on the effects of roentgen irradiation in 1949.

Definite standards of therapeutic criteria in rheumatoid arthritis were laid down in 1949 by Steinbrocker, Traeger, and Batterman.[35] They recommended that the response of rheumatoid arthritis to therapy should be divided into four grades. As our adjunct to this, supplementary aids in the form of classification of stages of rheumatoid arthritis and of functional capacity were incorporated in the evaluation of therapy. Division of the disease into stages according to radiological changes had previously been described in 1937 by Taylor.[36]

The general functional status of the patient was the main feature recommended in clinical assessment in a memorandum of the Nuffield Foundation on therapeutic trials in rheumatoid arthritis, by Kellgren and Duthie.[37]

The actual measurement of the clinical objective signs which constitute the therapeutic criteria mentioned by the above workers has been the subject of much work in the past few years. Most of the work has been done since attempts have been made to find substances which may have a beneficial effect, similar to that of ACTH and cortisone, originally described by Hench *et al.*,[38] who took immense pains to control and check their work. Measuring improvement in rheumatoid arthritis was discussed in a leading article in the *British Medical Journal* in 1950.[39]

Endeavours to evaluate joint tenderness have been made by most workers on the subject.[23, 40-44] The method used in all cases was to apply firm pressure over a joint, and the amount of joint tenderness was graded arbitrarily according to the patient's reaction. This method of assessing and grading joint tenderness was adopted by a joint committee of the Medical Research Council and the Nuffield Foundation for the investigation of the adjuvant effect of cortisone and ACTH on manipulation procedures in rheumatoid arthritis.[45] Steinbrocker[46] drew attention to the fact that routine digital palpation may be very inadequate and misleading, and recommended the use of a pressure gauge called a "palpometer" for quantitative palpation. A description of this had been given in a previous article.[47] Another type of pressure gauge was described by Janus[48] in which the joint was compressed between sponge-rubber cushions, the part tested being kept in a water bath at 35° C. to avoid error due to temperature of a kind described by Kellgren, McGowan and Hughes.[49] Duthie[42] estimated joint tenderness by wrapping a sphygmomanometer cuff around the joint and inflating it until pain was felt.

Measurement of joint swelling has been more controversial than that of joint tenderness. Quin and others[43] did not measure joint swelling as they were unable to establish a satisfactory method. Harris[50] expressed surprise at this and described a method in which three measurements were taken. By using one measurement over the maximum circumference of a joint, Currie and Will[22] found that a variation of up to 0.5 cm. may arise from experimental error. Hart and Clark[51] described the use of jeweller's rings to measure swelling of the proximal interphalangeal joints. Dresner *et al.*[52] measured changes in hand volume by water displacement, as a method of estimating swelling of the hand.

A "blind" measurement of the angles of flexion and extension of the knees was described by Bywaters *et al.*[23] Dresner and his co-workers[52] measured passive movement of joints with a goniometer. Goniometers for measuring range of joint motion were criticized by Wainerdi.[53] Further criticism was made by Loxton *et al.*[54] who considered that a photographic record of joint range was more accurate and permanent. Disadvantages in the use of goniometers were enumerated by Williams,[55] who devised a mathematical method of determining the angle of movement of a joint.

Some of the aforementioned workers[41-43] measured the power of grip using a sphygmomanometer cuff sewn to get a cylinder of constant size. Duthie[42] used the sphygmomanometer bulb. Wainerdi,[56] in an analysis of normal and asthenic grips, used a sphygmomanometer with a pædiatric-sized cuff. Janus[48] used a special canvas-and-rubber bag connected to a mercury manometer. Dresner *et al.*[52] measured grip using a spring dynamometer.

Several workers[23, 41-43] measured certain functions involving most joints of the body and associated with everyday life, by timing one or more of these set actions. In assessing the adjuvant effect of cortisone on manipulation of the knee-joint, the joint committee of the M.R.C. and Nuffield Foundation[45] advised the estimation of the time taken to do five complete flexion-extensions, and the measurement of strength of thrust of the knee using a spring balance. Duthie[42] measured functional capacity by a weight and pulley circuit. Dresner *et al.*[52] measured manual dexterity with a screw-plate test. They also used cinematograph films to measure progress of function. Filming certain standard movements before and after therapy was also used by Hench *et al.*[40] and Copeman *et al.*[41] Photography was considered to be the most accurate method of assessing changes in joint functions by Loxton *et al.*,[54] who employed an elaborate method involving the use of automatic still and ciné films.

Two additional methods of study were advised by Copeman and his colleagues:[41]

1. The use of a "Wirek" magnetic wire recorder, so that the interview between the observer and patient could be reproduced at a later date.
2. The patient's own assessment, taking "100" as baseline, figures above 100 indicating deterioration and those below 100 denoting improvement.

The importance of taking adequate precautions to avoid the effect of psychological factors and the difficulties due to the natural history of the disease was stressed by most of the aforementioned workers. That "placebo effects", i.e. effects produced by accompanying psychological responses when agents are administered, do occur has been demonstrated by Wolf.[57] The effects produced by psychological factors in a series of uncontrolled cases of rheumatoid arthritis treated with deoxycortone and ascorbic acid were shown by Clark.[58] The use of inert control substances, the identity of which is unknown to patient, observer, nursing staff and all in contact with the patient, was strongly advised by Clark, and controls were employed by him and other workers.[16, 23, 38, 40, 41, 43, 48, 52] Using controls in their therapeutic trial with deoxycortone and ascorbic acid, Quin *et al.*[43] took the added precaution of avoiding any reference to records of previous results, and the order of administration of control substance and agent under trial was selected at random. Bedford,[59] in a study of eight women with rheumatoid arthritis, showed that their condition varied hour by hour even though they were having no treatment, thus calling attention to the large "experimental error" which is present where clinical assessment is not backed by statistical control. The importance and need for the use of controls in medical research trials was emphasized by Ross,[60] who analyzed 100 consecutive and unselected current medical journal articles and found that no attempt was made to use a control group in 45% of the articles. The necessity for planned and controlled clinical trials has also been stressed by Bradford Hill.[61]

METHODS

Methods of assessment were used in therapeutic trials for the evaluation of endocrine

preparations, gold combined with a low salt diet, insulin hypoglycæmia, ACTH and cortisone, insulin hypoglycæmia combined with ACTH or cortisone, intra-articular cortisone and 3-hydroxy-2-phenylcinchoninic acid (HPC). These trials were done by the Rheumatism Research Unit of the South Western and Oxford Regions in the Royal National Hospital for Rheumatic Diseases, Bath, England, and the results have been published.[21, 62-66]

Six methods of assessment were used: (1) general clinical assessment (by the observer), (2) patient's own subjective assessment, (3) determination of activity index, (4) estimation of functional capacity, (5) use of instruments and mechanical aids, and (6) estimation of erythrocyte sedimentation rate and hæmoglobin.

1. General Clinical Assessment (by the Observer)

The general clinical assessment was designed to give an over-all clinical impression of the disease and its response to treatment. Attention was paid to the feeling of well-being, pain (including rest pain), stiffness, joint tenderness, swelling, heat, and range of movement, in addition to functional capacity as indicated by questioning about ability to perform ordinary everyday tasks. Improvement was indicated by either "one plus (+)", "two pluses (++)", "three pluses (+++)", "four pluses (++++)", or as a percentage change on a credit system (0 increasing to 100%). A debit scheme was also used, the baseline being 100 and improvement being deducted.

The total number of general clinical assessments carried out by the observer was 1,004 on 234 patients.

2. Patient's own Subjective Assessment

At the initial clinical examination before treatment, it was explained to the patient that he would be examined and assessed at intervals during treatment with a view to determining clinical progress. He was then asked to cooperate in this by deciding for himself the percentage of improvement or otherwise that might occur. In order to obtain trustworthy figures, it was essential to ensure that patients thoroughly understood what was required, and that their opinions were unbiased and uninfluenced by others. Furthermore, in order to ensure that the observer's figure was not influenced by that of the patient, the patient was requested not to divulge his figure until it was asked for, after the observer had reached his own conclusion and figure.

Sixty-six patients were asked to give an over-all estimate of progress, and the total number of subjective assessments was 511.

3. Determination of Activity Index

Activity index represented an attempt to give an absolute numerical value to the activity of the disease. It was obtained by grouping several criteria, each of which was divided into grade of severity as units (the higher the unit, the greater the activity), and adding the units together.

TABLE I.

Activity Index A	
Pain at rest	
Absent	0 units of activity
Insufficient to prevent sleep or require analgesics	1 unit of activity
Sufficient to prevent sleep and require analgesics	2 units of activity
Change in weight	
Stationary or increasing	0 units of activity
Slight loss (1 - 4 lb.)	1 unit of activity
Marked loss (more than 4 lb.)	2 units of activity
E.S.R. (Westergren in one hour)	
0 - 15 mm.	0 units of activity
16 - 40 mm.	1 unit of activity
over 40 mm.	2 units of activity
Hæmoglobin value	
11.8 g./100 ml. and over	0 units of activity
11.7 - 9.6 g./100 ml.	1 unit of activity
9.5 g./100 ml. and below	2 units of activity

Three forms of activity index were used:

1. Activity index A incorporated pain at rest, change in weight, sedimentation rate and hæmoglobin value. Each of these criteria was graded on a three-point scale as shown in Table I. This index was estimated in 216 assessments on 108 patients. The chief source of error was considered to be the use of loss of weight as a criterion, as this in itself is comparative and not absolute.

2. Activity index B comprised the same criteria as activity index A, except that joint tenderness was included instead of change in weight. Joint tenderness was graded on a three-point scale depending on the patient's response when firm pressure was applied on a joint, as shown in

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TABLE II.

ACTIVITY INDEX B	
Joint tenderness	
No tenderness on pressure	0 units of activity
Admission of tenderness on pressure	1 unit of activity
Wincing, withdrawal or exclamation on pressure	2 units of activity

Table II. This index was determined on 62 patients, observations being made in 204 assessments. Activity index B was also thought to be not ideal, because of the use of pathological tests which might not necessarily run parallel to clinical disease activity.

3. Activity index C incorporated clinical features only, viz. pain, joint tenderness, swelling, warmth, and some of the general aspects of the disease (lassitude, lack of appetite, vasomotor imbalance). The scale of grading of these criteria is shown in Table III. Estimations were made in 511 assessments on 66 patients.

4. ESTIMATION OF FUNCTIONAL CAPACITY

In addition to obtaining an impression of functional ability as part of the general clinical assessment, functional capacity was estimated in two other ways: (1) By timing set everyday actions, usually consisting of walking a set distance and putting on or taking off a certain garment. (2) By classifying functional status. This was done in accordance with the method described by Steinbrocker *et al.*[35]

TABLE III.

ACTIVITY INDEX C	
Pain	
No pain	0 units of activity
Pain on movement or weight-bearing	1 unit of activity
Pain at rest insufficient to prevent sleep or require analgesics	2 units of activity
Pain at rest sufficient to prevent sleep and require analgesics	3 units of activity
Joint tenderness (firm pressure over joint)	
No tenderness	0 units of activity
Admission of tenderness	1 unit of activity
Wincing or grimacing on pressure	2 units of activity
Withdrawal and grimacing on pressure	3 units of activity
Swelling (clinical observation only)	
No swelling	0 units of activity
Slight periarticular swelling	1 unit of activity
Obvious but not gross swelling	2 units of activity
Gross swelling	3 units of activity
Warmth (clinical palpation only)	
Absence of warmth	0 units of activity
Presence of warmth	3 units of activity
General aspects of rheumatoid disease	
Lassitude and/or easy fatigue	1 unit of activity
Loss or reduction of appetite	1 unit of activity
Vasomotor imbalance (cold and/or sweating extremities)	1 unit of activity

Timing everyday actions was carried out on 13 patients in 147 assessments, and functional status was classified in 511 assessments on 66 patients.

Functional capacity and rheumatoid activity do not necessarily run parallel, and it is considered that, of the two criteria, reduction of rheumatoid activity is of greater significance and represents the crucial basis for assessment.

5. USE OF INSTRUMENTS AND MECHANICAL AIDS

Certain instruments were used in an attempt to obtain quantitative measurements of certain physical signs. The following mechanical aids were used:

1. *The "algesiometer"* (Fig. 1).—This was used to measure joint tenderness. It was adapted from an ordinary tire-pressure gauge by inserting a spring inside the barrel and exerting pressure against the spring by the piston. A metal button was welded to the end of the piston and this was suitably padded. Pressure was applied to a tender area by this padded button until the patient became aware of pain, and the reading on the piston scale was noted. An average of three readings was taken. The instrument was used to measure joint tenderness in relation to the wrist and ankle joints.

2. *The sphygmomanometer.*—A sphygmomanometer was adapted to measure joint tenderness by wrapping the bag and sleeve around the joint in question, and pumping up the pressure slowly and uniformly until the patient became aware of pain. The level of mercury was then read and an average of three readings was taken. Measurement of joint tenderness in this way was carried out in relation to the knee joints.

3. *The tape-measure.*—A tape-measure was used to measure swelling on the knee joints at the level of the mid-joint of the patella, the line of measurement being marked with skin pencil or silver nitrate.

4. *The goniometer* (Fig. 2).—A goniometer was used to measure range of movement at the knee, elbow, shoulder and hip joints. The instrument consists of two metal arms hinged together, one carrying a protractor and the other a pointer at the hinged ends. The pointer moves

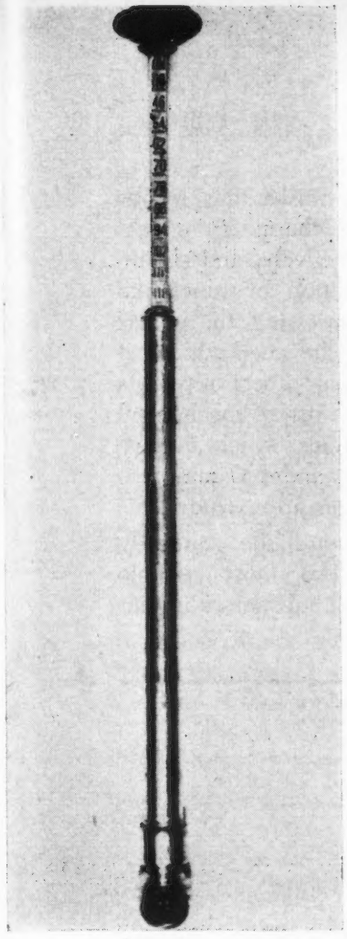


Fig. 1.—The algesiometer. Adapted from an ordinary tire-pressure gauge, and used to measure joint tenderness.

over the protractor scale, so giving a direct measurement of the angle between the two arms. In addition to the use of this instrument, "blind" measurements were also taken, using two strips of wood hinged together and aligned to the bony points. The angle was then drawn on paper and measured later.

5. *The "mercurial ergometer"* (Fig. 3).—This was used to measure strength of grip. It consists of a double bellows connected to a mercury manometer. The former comprises a rubber bulb connected to a thin-walled rubber bag. By means of the bulb, the bag can be inflated to a size most suitable to the patient's grip, and at the same time it will mould itself to the patient's hand. Using the same baseline level of mercury at each assessment for a particular patient, the patient was instructed to grip the bag slowly and steadily to the maximum possible. The height of the mercury was then read and an average of three readings was taken.

These instruments were used in a group of 13 patients. The number of clinical assessments carried out in this group was 193. The number of cases and assessments in which the instruments were used varied, as their use was restricted to those joints where the appropriate measurements were applicable.

6. ESTIMATION OF ERYTHROCYTE SEDIMENTATION RATE (E.S.R.) AND HÆMOGLOBIN

The E.S.R. was determined by the Westergren method. Hæmoglobin was determined by the M.R.C. Grey-Wedge Photometer. These pathological tests were done before, during and after treatment on 216 patients, estimations being made at 532 assessments.

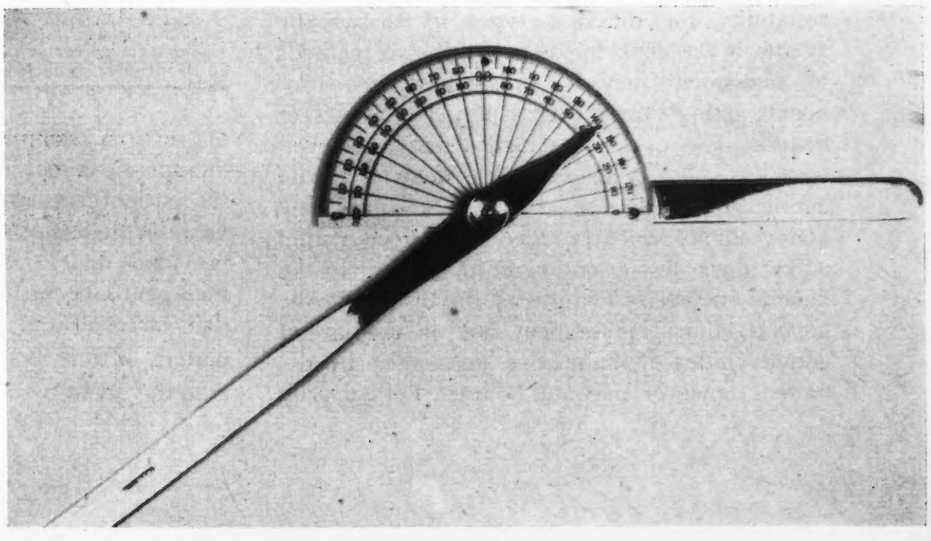


Fig. 2.—The goniometer. Used to measure range of joint movement.

RESULTS AND CONCLUSIONS

In order to determine the degree of association between the methods used, correlation coefficients (r) were calculated. The coefficients of correlation were determined for series of corresponding values of clinical change as recorded by the observer, and changes as recorded by each of the other methods of assessment in turn. The results of the correlation coefficients are given in Table IV. In those methods where several groups of observations have been made, it has been possible to calculate more than one coefficient, and these are arranged according to magnitude. The significant correlation coefficients are denoted by an asterisk. It will be seen from the table that the great majority of the coefficients are significant of an association between the observer's clinical assessment and the other methods of assessment used. Only four out of 27 coefficients are not significant. The most intensive of all the associations is that between clinical change recorded by the observer and clinical change as assessed by the patient. The correlation coefficient for a series of 511 corresponding values is +0.83, which is highly significant and higher than any of the other significant coefficients which vary from +0.19 to +0.59. This suggests that, as far as an over-all estimate of clinical change following treatment is concerned, the patient's own figure is closely related to that of the observer and may be relied on.

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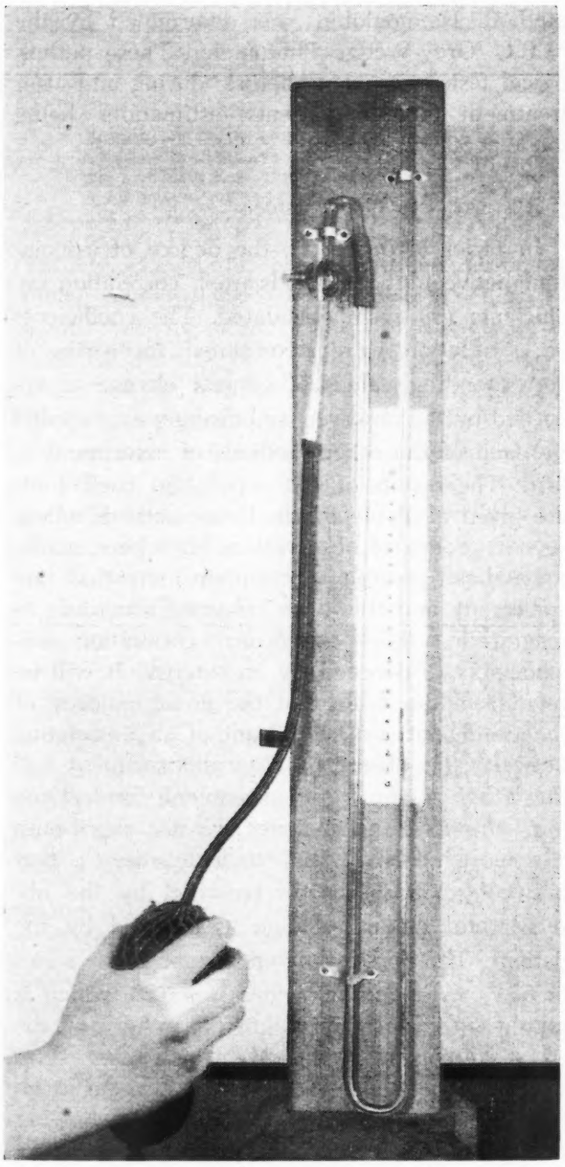


Fig. 3.—The mercurial ergometer. Used to measure strength of grip.

Analyzing the methods with regard to their suitability for different types of therapeutic agents, it was considered that all the six methods of assessment may be satisfactorily used for agents acting slowly over a period of weeks or months. The use of mechanical aids, however, is of less value in assessing the effects of a drug acting on the disease as a whole. In rapidly acting agents which produce their effects within a few days, less attention need be paid to the general subjective features of the disease in the general clinical assessment and in the use of activity index C. Subjective assessment by the patient, however, may still be used. Both activity indices A and B may give misleading results because of incorporation of change in weight and pathological tests, respectively, and should not be used. The classification of functional status is of little value in assessing the effects of agents acting rapidly. The methods most suitable for assessing the local effects of agents applied to a joint include the use of mechanical aids, and timing those actions which involve the joint in question. Activity index C may also be used if the general features are excluded.

All therapeutic trials should be carefully planned and controlled. The most reliable method of using inert control substances is that of random sampling, whatever the type of therapeutic agent used. The method in which the patient acts as his own control is of some value in the assessment of agents acting rapidly, provided that patients are transferred from therapeutic agent to control and vice versa, and that both substances are given for equivalent periods of time. In using controls, it is important that the identity of inert substance and agent

TABLE IV.

LIST OF CORRELATION COEFFICIENTS (r)

Clinical change (observer) with clinical change (patient)	511 assessments	r = +0.83*
Clinical change (observer) with activity index		
Activity index C	511 assessments	r = +0.59*
Activity index B	204 "	r = +0.58*
Activity index A	216 "	r = +0.32*
Activity index B with activity index C	120 assessments	r = +0.55*
Clinical change (observer) with functional capacity		
Timing set actions	147 assessments	r = +0.44*
Classifying functional status	511 "	r = +0.34*
Clinical change (observer) with mechanical aids		
"Algesiometer" (L. ankle)	128 assessments	r = +0.59*
Goniometer (L. elbow)	89 "	r = +0.58*
Sphygmomanometer (R. knee)	131 "	r = +0.55*
"Mercurial ergometer" (R. hand)	125 "	r = +0.55*
"Algesiometer" (R. ankle)	128 "	r = +0.49*
Goniometer (R. shoulder)	70 "	r = +0.49*
Goniometer (R. elbow)	69 "	r = +0.43*
"Mercurial ergometer" (L. hand)	125 "	r = +0.41*
Tape-measure (R. knee)	165 "	r = +0.39*
Sphygmomanometer (L. knee)	127 "	r = +0.36*
Goniometer (R. knee)	165 "	r = +0.29*
"Algesiometer" (L. wrist)	169 "	r = +0.26*
"Algesiometer" (R. wrist)	148 "	r = +0.21*
Tape-measure (L. knee)	167 "	r = +0.097
Goniometer (L. shoulder)	61 "	r = −0.066
Goniometer (L. knee)	167 "	r = −0.046
Clinical change (observer) with sedimentation rate		
Clinical change expressed in units and change in sedimentation rate expressed in mm. Westergren		r = +0.41*
Clinical change and change in sedimentation rate expressed as percentage change	532 assessments	r = +0.23*
Clinical change (observer) with hæmoglobin		
Clinical change expressed in units and change in hæmoglobin expressed in grams per 100 ml.		r = +0.19*
Clinical change and change in hæmoglobin expressed as percentage change	532 assessments	r = −0.053

*Statistically significant.

under trial should be, as far as possible, unknown to both patient and observer.

SUMMARY

In view of the difficulties associated with the evaluation of therapeutic agents in rheumatoid arthritis, an attempt has been made to find suitably controlled methods of assessment which would show whether or not a beneficial effect was due to an agent under trial.

Six methods of assessment were used. These included a general clinical assessment by the observer, the patient's own assessment, the determination of an index of activity, the estimation of functional capacity, the use of instruments, and the estimation of sedimentation rate and hæmoglobin value.

The degree of association between these methods was determined by the calculation of correlation coefficients. The results of these calculations showed that the great majority of coefficients were significant of an association between the observer's clinical assessment and the other methods of assessment used. The most intensive of all the associations was that between clinical change recorded by the observer and clinical change as assessed by the patient. This suggests that the patient's figure is closely related to that of the observer.

Methods of assessment will depend on the rapidity of action of the agent under trial, and on its local or general use.

Whatever methods are used for assessment in therapeutic trials, all such trials should be carefully planned and controlled.

I am indebted to Dr. G. D. Kersley for encouragement, advice and helpful criticism in carrying out this work; to Dr. H. J. Gibson for the results of the pathological tests; and to Dr. G. Herdan of the University of Bristol for help in the statistical analysis.

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TEN-YEAR PROGNOSIS OF ACUTE MYOCARDIAL INFARCTION

A group of patients who had recovered from their presumed first myocardial infarction and who lived more than two months were followed up for a period of 10 years. A survival period of two months was selected since, by this time, the majority of patients who recover will have become ambulatory and are usually ready to resume a modified or regular routine of life. Only patients with characteristic clinical and electrocardiographic evidence were selected.

Of the 211 patients who fell within the criteria of the study, one-third lived more than 10 years. The majority of those who died did so in the first five years. The major cause of death (88%) was cardiovascular disease.

A life expectancy of more than 10 years after a myocardial infarction is more common in younger individuals than in the older age group. It appears that the patient who has made a good functional recovery is likely to live longer than those disabled by congestive heart failure, angina pectoris or a cerebral embolism.

Three-fourths of the patients made a complete or partial economic recovery.—M. M. Weiss: *Am. J. M. Sc.*, 231: 9, 1956.

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DEPRESSIVE STATES DURING RAUWOLFIA THERAPY FOR ARTERIAL HYPERTENSION*

A REPORT OF 30 CASES

GUY LEMIEUX, M.D.,
ANDRE DAVIGNON, M.D.† and
JACQUES GENEST, M.D., F.R.C.P., F.A.C.P.,
Montreal

DURING THE PAST YEAR, several reports[1-10] have appeared in the medical literature on the occurrence of mental symptoms during rauwolfia therapy for arterial hypertension. All these reports are concerned with only a very small number of patients, and the relationship between the occurrence of mental changes and the administration of rauwolfia has not been clearly established.

During the last 18 months, we have been able to observe 30 patients with depressive states during rauwolfia therapy for arterial hypertension. A study of these cases seems to indicate a definite relation between rauwolfia administration and mental symptoms.

Between June 1954 and December 1955, 296 patients were treated and seen regularly at our Hypertension Clinic. All these subjects had been previously admitted to the Hôtel-Dieu Hospital where a complete clinical investigation including evaluation of the cardiac, vascular, renal, cerebral and ophthalmoscopic status had been done in each case. After discharge, the patients were seen at weekly, fortnightly or monthly intervals.

Of these 296 patients (Table I) 101 took no rauwolfia preparations; they received either hydralazine (Apresoline), hexamethonium, or pentolinium (Ansolysen) alone or in combination.

The remaining 195 patients took rauwolfia preparations, either alone or in combination with the already mentioned drugs. Of these 195 patients, 134 subjects took reserpine (Serpasil, Serpiloid or Rau-Sed) and the remaining 61 took a whole root preparation (Raudixin) or the purified alkaloidal fraction also called the alseroxylon fraction (Rauwiloid).‡

TABLE I.

PATIENTS TREATED FOR ARTERIAL HYPERTENSION: JUNE 1954 - DECEMBER 1955

Total number of patients	296
Taking no rauwolfia	101
Taking rauwolfia†	195
Reserpine	134
Whole root or alseroxylon fraction	61

RESULTS

Among the 101 patients receiving no rauwolfia preparations, no subject developed any mental symptoms during therapy, whereas 30 out of the 195 patients under rauwolfia therapy showed a depressive state. Of these 30 patients, 24 were females and 6 were males. The age ranged from 33 to 70 years, with an average of 52.7 years. The clinical diagnosis of hypertensive state was as follows: essential hypertension 27 cases (18 benign, 4 severe and 5 arteriosclerotic), malignant hypertension 2 cases, and hypertension of renal origin 1 case (Table II).

The incidence of mental depression among the total number of patients is 10%. Fifteen per cent of all the patients receiving rauwolfia therapy had mental changes. Of the 30 patients who developed depressive states, 25 were under reserpine (83%)—18% of all subjects treated with this alkaloid. The remaining 5 were under whole root extract or alseroxylon fraction—8% of all patients treated with these agents.

The lapse of time between the administration of the drug and the appearance of mental symptoms is illustrated in Tables II and V. With reserpine, it ranged from 2 weeks to 14 months with an average of 4½ months. With the alseroxylon fraction, 5 months of therapy elapsed before the appearance of mental symptoms. When whole root extract was used, the lapse of time ranged from 2½ to 3 months with an average of almost 3 months.

The daily dosage of reserpine used ranged from 0.75 to 4 mg. and averaged 1.36 mg.; with the alseroxylon fraction, it ranged from 8 to 12 mg. and averaged 10 mg.; with the whole root extract, it ranged from 150 to 200 mg. with an average of 183 mg. (Tables II and V).

Clinically, the picture was that of mental depression, although two patients under reserpine (E.B. and W.L.) had definite psychotic reactions. The most frequent complaints were a

*From the Clinical Research Department, Hôtel-Dieu Hospital, Montreal. Work supported through grants from the Department of National Health and Welfare, Ottawa, and the Ministry of Health of Quebec (Federal-Provincial Plan) and the Ciba Company, Montreal.
†Fellow of the National Research Council 1954-1955.
‡Rauwolfia preparations were kindly supplied to us through the courtesy of Dr. Walter Murphy, Ciba Co., Montreal (Serpasil); Mr. A. Garstone, Riker Pharmaceutical Co. Ltd. (Serpiloid and Rauwiloid), and Mr. J. H. Comte, E. R. Squibb & Sons of Canada Ltd. (Raudoxin and Rau-Sed).

TABLE II.

DEPRESSIVE STATES DURING RAUWOLFIA THERAPY

Patient	*Age*	*Sex*	*Arterial hypertension*	*Duration of therapy (months)*	*Daily dosage (mg.)*	*Severity of depression (grade I to IV) H = hospitalization*
					Reserpine	
R.L.	47	F.	Benign essential	6	1 - 2	II
F.R.	33	F.	Severe essential	3½	1	II
F.P.	43	F.	Malignant	3	0.75	IV
S.S.L.	70	F.	Arterioscl.	6½	1 - 1.5	II
N.A.L.	50	F.	Benign essential	½	4	III
V.K.	46	F.	Benign essential	6	0.5 - 1.5	III
G.M.	46	M.	Malignant	8	0.75 - 1.5	III
H.P.	63	F.	Severe essential	6	0.75	IV *H*
C.S.P.	53	F.	Benign essential	3	1.5	IV
L.P.	48	M.	Benign essential	5	1.5 - 3	IV *H*
E.B.	54	F.	Benign essential	7½	0.75 - 1.5	IV *H*
H.R.	56	F.	Benign essential	4	1.5 - 2	IV
C.R.	62	F.	Severe essential	4	1 - 1.5	III
P.L.	69	F.	Arterioscl.	3½	1 - 1.5	IV *H*
Y.H.	46	F.	Benign essential	4	1	IV
E.F.	56	F.	Benign essential	2	0.75	IV *H*
O.B.	58	M.	Benign essential	7	0.75 - 3	III *H*
J.E.L.	46	F.	Benign essential	6	2	IV *H*
E.S.	63	M.	Benign essential	4	1.5	II
I.M.	56	F.	Benign essential	½	1	III
E.R.	56	F.	Benign essential	5	1	III
A.L.	68	F.	Arterioscl.	½	1.5	III
D.R.	49	M.	Renal	2	0.75	IV *H*
W.L.	42	F.	Benign essential	3	0.75 - 1.5	IV *H*
E.P.	36	F.	Severe essential	14	0.75 - 1.5	III
					Alseroxylon Fr.	
J.P.	56	F.	Benign essential	5	12	IV *H*
P.B.	53	M.	Benign essential	5	8	II
					Whole root	
M.S.O.	38	F.	Benign essential	3	150 - 200	III
J.A.L.	55	F.	Arterioscl.	3	150 - 200	III
A.B.	64	F.	Arterioscl.	2½	200	III

TABLE III.

DEPRESSIVE STATES DURING THERAPY FOR ARTERIAL HYPERTENSION

Total number	30	100%
Taking no rauwolfia	0	0%
Taking rauwolfia	30	100%
Taking reserpine	25	83.3%
Taking the whole root	3	10%
Taking the alseroxylon fraction	2	6.6%

feeling of sadness and discouragement with lack of ambition and energy, crying spells without motivation, loss of interest in usual activities and worry over trifles (Table VI). Anxiety was not a constant feature, although it was definite in 9 cases. Other symptoms included weakness and fatigue, phobias, decreased appetite, insomnia,

TABLE IV.

INCIDENCE OF DEPRESSIVE STATES DURING RAUWOLFIA THERAPY

Total number (30 out of 296)	10%
Under rauwolfia (30 out of 195)	15%
Reserpine (25 out of 134)	18%
Whole root or alseroxylon fraction (5 out of 61)	8%

TABLE V.

DEPRESSIVE STATES DURING RAUWOLFIA THERAPY

	Average duration of therapy (months)	*Average daily dosage (mg.)*
Reserpine (25 cases)	4.5 (½ to 14)	1.36 (0.75 to 4)
Alseroxylon fraction (2 cases)	5	10 (8 to 12)
Whole root (3 cases)	2.8 (2½ to 3)	183 (150 to 200)

suicidal thoughts and vague somatic complaints. The two patients with psychotic reactions had agitation, mental confusion and delusions.

The severity of the mental syndrome was graded from I to IV depending on the intensity of symptoms (Table II). Only cases with definite mental changes are included in this series. Ten of the 30 cases required admission to the hospital and close psychiatric treatment. In these cases psychiatric diagnosis was as follows: depressive state 7, anxiety state 1, and melancholia 2. The other moderately severe cases received psychiat-

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TABLE VI.

DEPRESSIVE STATES DURING RAUWOLFIA THERAPY: SYMPTOMS (30 CASES)

Most frequent	*Less frequent*
Feeling of sadness and discouragement	Suicidal thoughts
Crying spells	Confusion
Loss of interest	Agitation
Worry over trifles	Delusions
Weakness and fatigue	Self-accusation
Phobias	Obsessive thinking
Anxiety	
Decreased appetite	
Vague somatic complaints	
Insomnia	

ric care in the outpatient clinic of the department of neuropsychiatry.

The management of the mental condition which developed under rauwolfia therapy is illustrated in Table VII. Complete cessation of administration of the drug in 19 cases resulted in total recovery in 11 patients, marked improvement in 7 and no improvement in 1 patient (P.L.) Reduction in dosage in 6 cases produced complete recovery in 4 cases, marked improvement in 1 and no effect in 1 subject (J.P.) who now manifests features of severe hypochondria. Electroshock therapy was administered to 5 patients with total recovery in 3 cases, marked improvement in 1 and no improvement in 1 patient (O.R.), who remains depressed and anxious after two courses of shock therapy.

TABLE VII.

MANAGEMENT OF DEPRESSIVE STATES DURING RAUWOLFIA THERAPY (30 CASES)

	Complete recovery	*Marked improvement*	*No improvement*
Complete cessation of the drug (19 cases)	11	7	1
Reduction in dosage (6 cases)	4	1	1
Electroshock therapy (5 cases)	3	1	1

The period of time between the depressive state and recovery ranged from ½ to 3 months after cessation of the drug or reduction in dosage. Following electroshock therapy, recovery was much more rapid, demanding an average course of six treatments.

Seven patients who had developed a depressive state under reserpine therapy and who had completely recovered after cessation of the drug were again given reserpine at the former dosage. No relapse occurred in four patients after 1 to 4 months, while in the remaining three patients a relapse was noted 15 days to 2 months after resumption of reserpine; the mental symptoms disappeared rapidly with reduction in dosage.

Too much space would be needed to give an abstract of the history of each of our 30 cases. However, the following examples illustrate the clinical features of the depressive states encountered during rauwolfia therapy.

1. A 53-year-old woman (C.S.P.) with benign essential hypertension (average B.P. 210/110 mm. Hg) was given reserpine 1.5 mg. daily from July 27, 1954. Towards the end of August, she complained of occasional crying spells without motivation. On October 22, 1954, after three months of reserpine therapy, she began to feel depressed. She worried over trifles and complained of insomnia. There was no evident emotional problem and no history of previous mental depression. Reserpine was reduced to 1 mg. per day. On November 19, her depressive state became more accentuated. She felt sad and discouraged. She had crying spells without motivation every day. She complained of anorexia, loss of weight and insomnia; she stated that her food could not reach her stomach and she had much difficulty in swallowing. Complete x-ray studies of the digestive tract revealed no abnormality. The patient had lost interest in her previous activities; she could no longer read or pay attention to the radio or television. She also feared she was losing her mind, and that she had a serious disease such as cancer. On November 26, reserpine was reduced to 0.5 mg. per day, and amphetamine with mephenesin were given by the consulting psychiatrist.

By January 14, 1955, the mental symptoms had completely disappeared and the patient has been feeling well since then and is still taking 0.5 mg. reserpine a day.

2. A 48-year-old man (L.P.) with benign essential hypertension (average B.P. 230/140 mm. Hg) was given 300 mg. hydralazine and 1.5 mg. reserpine a day from August 6, 1954. Under this regimen, there was a significant lowering of the blood pressure to 180/110. On December 15, 1954, reserpine was increased to 3 mg. a day. On January 10, 1955, the patient was admitted to hospital in a severe depressive state. He felt like crying all the time; he also felt lonely and very sad. He was anxious, feared he would die suddenly and was afraid of walking alone. He complained of a feeling of pressure all over his head. Other complaints were of nausea, loss of appetite and inability to sleep well. The patient kept thinking of his parents and felt sorry for them because they were getting old. He had lost interest in reading or listening to the radio. He had a long history of emotional conflicts. Reserpine was ceased completely and a neuropsychiatrist was called in consultation. The patient improved rapidly with psychotherapy and amphetamine. On March 5, 1955, he was discharged on 100 mg. hydralazine a day. On March 18, 0.5 mg. reserpine a day was added. On April 15, the patient felt depressed again. Reserpine was discontinued and three weeks later the patient felt well with 400 mg. hydralazine a day. No relapse has occurred since then.

3. A 56-year-old woman (H.R.) with benign essential hypertension (average B.P. 240/120 mm. Hg) took 1.5 to 2 mg. reserpine daily from September 10, 1954, to January 7, 1955, at which time she developed a depressive state. She felt sad, discouraged, lonely and wished to remain alone. She also complained of insomnia and loss of interest in her previous activities. Reserpine was discontinued but the patient became progressively worse and psychotherapy provided no significant help. After a course of six electroshock treatments, the symptoms had completely disappeared. On March 4, 1955, reserpine was given again but at a lower dosage (0.5 mg. a day) with pentolinium and hydralazine. The patient has been well since.

4. A 62-year-old woman (C.R.) with severe essential hypertension (average B.P. 260/130 mm. Hg) took 1.5 mg. reserpine a day from September 24, 1954, to February 9, 1955. A depressive state then developed with crying spells, fatigue, worry over trifles, fear of staying alone and of losing her mind, and loss of interest in her previously enjoyed social activities. Reserpine was reduced to 0.75 mg. a day and on April 6, 1955, all the mental symptoms had disappeared with no relapse since then.

5. A 54-year-old woman (E.B.) with benign essential hypertension (average B.P. 220/120 mm. Hg) took 1.5 mg. reserpine a day during 7½ months, after which period an acute psychotic reaction developed. The patient felt sad and lonely and at times became agitated and confused. In the hospital, reserpine was reduced to 0.75 mg. per day and electroshock therapy was instituted. Three weeks later, she felt well and left the hospital. She has been taking 0.75 mg. reserpine a day since then, with no relapse.

DISCUSSION

We think that the present study of 30 cases of depressive states during rauwolfia therapy seems to clearly incriminate the latter drug in the production of mental symptoms. At first glance, reserpine seems to be the most active agent, as 83% of all our cases were under therapy with this drug and it may be logical to assume that the reserpine contained in the whole root extract or the alseroxylon fraction is responsible for these mental changes. However, the high incidence of mental depression during reserpine therapy may be due to the relatively much higher dosages used with this drug, as compared with whole root extract and the alseroxylon fraction. Had equivalent dosages of the latter drugs been used, the incidence of mental changes might have been the same during therapy with these agents. This aspect of the problem is now being studied at our clinic; reserpine is being given in doses of less than 0.6 mg. a day in order to find out whether the same hypotensive action can be obtained with a lower incidence of mental depression.

In evaluating the factors involved in the production of such mental changes, we could not detect any relationship between the hypotensive effect of rauwolfia and the occurrence of depressive states. It must also be remembered that in the 101 patients who received more potent hypotensive drugs like hydralazine, hexamethonium and pentolinium without rauwolfia, no depressive states were encountered.

The dosage used is certainly an important factor, for the average daily dosage in our patients exceeded that usually recommended; furthermore, reduction in dosage frequently resulted in complete recovery. However, many patients receiving larger doses of rauwolfia had no depressive symptoms, so that dosage cannot be considered as the sole important factor.

Duration of therapy averaged four months and seems to be another factor. But it must not be forgotten that some individuals developed a depressive state after only 15 days of therapy and some after periods of seven or even 14 months. Moreover, some patients have taken rauwolfia for 18 months and more without developing any mental depression.

The age of our patients might be another factor. The average age was 52.7 years, with the great majority past 50 years. Mental depression is mostly encountered in this age group, and rauwolfia might precipitate the development of mental depression during this period of life.

Individual susceptibility and pre-existing personality could well be another very important factor. Amongst our 30 patients 10 had evidently disturbed personality with apparent anxiety, features of hypochondria or a history of previous depressive moods and mental depression. Complete personality studies were made on only a few patients; we think that this factor should be thoroughly investigated during further studies.

We now feel that before instituting rauwolfia therapy in any case, a complete history regarding any previous mental depression or depressive moods should be obtained, especially if the patient is in the fifth decade of life or more. Rauwolfia preparations should be given with great caution if a tendency to mental depression is discovered. In any given case, the dosage prescribed should be as low as possible and probably under 0.75 mg. a day if reserpine is used. Other hypotensive agents should be resorted to, if rauwolfia fails to lower the blood pressure with this dosage.

SUMMARY AND CONCLUSIONS

1. During an 18-month period, 10% of all our patients treated for arterial hypertension developed a depressive state.

2. All these patients were under rauwolfia therapy.

3. The mental changes subsided after reduction in dosage or complete cessation of the drug, but sometimes required admission to hospital and electroshock therapy.

4. The most important factors in the production of these symptoms seem to be the dosage

used, the duration of therapy and probably the age, the susceptibility and the pre-existing personality of the patient.

5. Rauwolfia preparations should probably be given with great caution to patients with a previous history of mental depression, especially if they are in the fifth decade of life or more.

6. These agents should be used at the lowest effective dosage for the reduction of blood pressure. If reserpine is used, the dosage should be under 0.75 mg. a day.

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RÉSUMÉ

Les auteurs ont été à même de suivre une série de 296 hypertendus dont 195 recevaient une préparation quelconque de Rauwolfia. Alors qu'aucun des 101 ne recevant pas de Rauwolfia n'accusa de trouble mental, 30 de ceux qui en reçurent montrèrent un état dépressif. Ces symptômes se manifestèrent dans une moyenne d'environ 4 mois après le début du traitement. Les doses étaient supérieures à celles communément employées. Dix de ces malades durent être admis à l'hôpital pour y subir des traitements psychiatriques. La plupart s'améliorèrent, plusieurs même guérirent complètement à la simple diminution de la dose ou à la suppression de la Rauwolfia; cependant, un cas se montra rebelle à deux séries d'électrochocs. La thérapie fut reprise avec rechute dans certains cas et bonne tolérance dans d'autres. Il semblerait que l'âge des malades ainsi que les traits de leur personnalité soient des facteurs d'aussi grande importance dans le développement de ces troubles que les doses de médicament employées. M.R.D.

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PSYCHOSIS AND ENHANCED ANXIETY PRODUCED BY RESERPINE AND CHLORPROMAZINE*

G. J. SARWER-FONER, B.A., M.D. and W. OGLE, B.A., M.D., *Montreal*

WE FIRST REFERRED to the production of psychosis by reserpine and chlorpromazine in our preliminary report on the use of reserpine† in psychiatric patients.[8] Freis,[3] Doyle[2] and other authors[4, 5, 12] had previously mentioned mainly depressive reactions and an occasional anxiety reaction, as occurring in patients treated, on a long-term basis, with reserpine for essential hypertension. Recently, other authors[1, 6, 11] have reported psychotic depressions occurring during treatment for essential hypertension with reserpine. These latter authors have emphasized these reactions, whereas earlier authors, with the exception of Freis, had not done so. We believe our work to be the first dealing specifically with psychiatric patients, and offering an explanation of the mechanisms involved in these reactions. To our knowledge, it is also the first to implicate chlorpromazine as well as reserpine.

In a study of the physiological and psychological effects of reserpine on affect, 55 carefully selected psychiatric patients were intensively studied over a one-year period (July 1954 to July 1955). The research design was novel.[8, 9] The data and conclusions of this study have been reported in detail elsewhere.[8-10] Concomitantly chlorpromazine was used in 35 cases on a non-research basis, i.e. when indicated as an ordinary drug. Sixteen out of the above-mentioned groups are the subject of this paper, because they were characterized by the same general reaction types and by common psychodynamic elements. The present paper consists of a detailed report of these cases, a discussion of the factors involved, and a statement of how we believe this phenomenon is produced.

Dose: The average dose of reserpine in the 55 cases was 7 mg. daily orally or intramuscularly. The average duration of treatment was 26 days. For chlorpromazine the dose was 50-100 mg. three or four times a day orally or intramuscularly. Duration of treatment varied greatly in the 35 cases.

*From the Department of Psychiatry, Queen Mary Veterans Hospital, Montreal and the Department of Psychiatry, McGill University, Faculty of Medicine.
†Supplied as Serpasil through the courtesy of Dr. C. W. Murphy, Medical Director, Ciba Company, Ltd.

Intensive knowledge of the psychodynamics and interpersonal relations has enabled us to formulate opinions as to the psychological as well as the physiological factors involved in the psychic reactions.

PRODUCTION OF PSYCHOSIS OR OF FURTHER PSYCHOTIC DISINTEGRATION WITH RESERPINE. (B.P., P., R. = blood pressure, pulse and respiration.)

1. (Case 11). G.A., a 25-year-old man. Before receiving reserpine, he showed perplexity, indecision, ambivalence and ambitendency. He could not make up his mind as to the proper course, was somewhat sad and unhappy, and had a bland expression. He was anxious, but masked all the above with a great need to move around, be tremendously active, and unrestrained in his motor activity, such as drinking, going out, cashing bad cheques or running up debts. His symptoms developed when he was removed from his paratrooper's job, involving frequent jumping, to one requiring very little actual duty or activity in a newly forming regiment. When frustrated in his outgoingness by being confined to the ward, he became increasingly tense and showed an inappropriate euphoria. He was given 2.5 mg. reserpine intramuscularly four times a day for two days, and 3 mg. orally four times a day for 11 days. Weight went from 210 to 218 lb. in seven days, stabilizing at 218 lb. There was no œdema. His appetite had been good, but the patient complained that he lost his "zest in eating" while on the drug. Blood pressure fell from 125/70 to 125/70-90/40, depending on the dose, stabilizing around 100/60 mm. Hg. Pulse rate fell from 80 to 60 (variation 80-56); respiration rate remained at 20. The patient felt that he was "worse". The results in respect of affect were considered poor. The patient was slowed down; his motor activity was markedly cut; he was tired, drowsy and irritable, and felt "held down". He could move his body, but tended to move it in one block, although he was able to do otherwise. He was unhappy, jittery and extremely anxious. He felt cut off from life, "unable to sleep, unable to stay awake". He felt he was "going queer", felt cut off "from outside things", and felt that his body was changing. Main observable changes were slowing down, inappropriate euphoria, panic at being chemically held, and a feeling of change and dissociation and of changes in body image and in his motor control. The natural course of the disease was changed for the worse; from an acting out person who mastered his anxiety through activity, he became an inhibited, unhappy frustrated man whose mental content became psychotic. The side-effect was nasal stuffiness. The patient was taken off the drug, and returned to his pre-drug state within a week. He was a very happy and relieved man at this, and remained with his acting out behaviour for the remaining month in hospital.

Comment: The drug removed his ability for vigorous motor activity at all levels. This rendered him more passive and he felt this as a lessening of his masculine prowess. He became paranoid.

2. (Case 16). S.O., aged 33, before receiving reserpine showed the beginnings of motor overactivity, flight of ideas, a tendency to dissociated thinking and a mild euphoria. He was aware that this was an abnormal state. On admission he was dependent, clinging, shaking hands, and speaking pleasantly to everyone. He was inclined to be passive in his interpersonal relations, and was open to verbal reassurance with good temporary effect. He had religious delusions and illusions, and grandiose ideas, and showed perplexity at his state, ambivalence, and ambitendency. His normal premorbid personality was marked by considerable drive in all activities and by social outgoingness. Physical findings were normal. Dosage: he received 5 mg. i.m. b.i.d. stat, then 5 mg. i.m. t.i.d. for three days, then q.i.d. for two days. He received one extra 5 mg. i.m. dose on the last day. Weight went from 124 to 129 lb. in six days. No œdema. His appetite changed from poor to good. His B.P., pulse and respiration were 130/90, 112, 20 before receiving the drug and 130/90-90/60, 88-72 and 20 while on the drug. B.P. fluctuated with dose and averaged 100/70. Patient felt he was "not helped". The result on affect was considered poor. Patient became calm and drowsy and felt held down. He was able to battle with his delusions, grandiosity and disorientation. His flight of ideas stopped. His irritability and impulsivity remained. Thus, the initial effect was excellent, but only enough drug to calm him had been given, the aim being to permit him to be up and around. When an extra dose which cut his activity to a level that immobilized him was given, he became paranoic, fearful, agitated and suicidal. He feared a plot against him, he felt that things had changed. He couldn't move, he felt we were changing him, and he became afraid that he would have to kill himself. The natural course of the disease was unchanged. The patient moved head, trunk and upper limbs in one block when under the influence of the last dose. Because of his condition he was transferred to a closed hospital. Final diagnosis: schizophrenia, schizo-affective type.

Comment: This man had an early psychotic process which he was able to cope with as long as he had motor activity as a defence. His defensive mobility was chemically removed, and greater psychotic deterioration resulted.

3. (Case 45). J.R., aged 34, before reserpine treatment had marked anxiety. He was trembling, sweating, scratching, moderately sad and markedly irritable. There was dermatitis eczematoides, interdigital dermatitis, and low back pain without physical signs. Dose: 7 mg. daily p.o. for 21 days. He gained 5 lb. in 21 days. No œdema. Appetite remained fair. B.P., P. and R. before reserpine treatment 130/80, 90, 20; on drug, B.P. fell to 100/70 in a day, then fluctuated between 140/90 and 90/50, P. 90 to 68, R. 20. Patient felt he was "not helped". Results on affect were considered poor; the patient was slowed, lost his tremor, sweating, irritability and sleeplessness. He appeared less sad. The low back pain was unchanged, but he developed bowel symptoms which persisted, and marked projective thinking. Major observed changes were that he appeared slowed, tired, sleepy and drowsy. His ability to relate in the interpersonal field was reduced. The natural course of disease was changed for the worse; from obsessive compulsive state, with signs of anxiety and with somatization, to loss of anxiety but also loss of ability to function positively. He felt passive and frightened. He developed more somatic symptoms, and paranoid (projective) thinking. Side-effects were stuffiness in nose, nausea, and on one occasion hiccups. The patient was taken off the drug and given sub-coma insulin and supportive psychotherapy; he showed a little symptomatic improvement in 1½ months.

Comment: Here again the physiological effects of chemically "holding him down" were intensely threatening, and resulted in psychosis.

4. (Case 48). A.A., aged 38, complained of sleeplessness, headache, bowel complaints, and itching around the anus and genitals. Few overt signs of anxiety. He was thin, with dermatitis around anus, genitals and knees. Dose: 2 mg. daily for 15 days. He gained 3 lb. in 15 days. No œdema. Appetite changed from poor to fair. B.P. 140/80 before drug; on drug fluctuated from 140/80 to 100/50. P. fell from 90 to 60, R. remained at 16. Patient felt he was "helped". For one week patient slept better and was uncomplaining. He was quiet, was slowed, felt tired, and was socially more co-operative and outgoing. His activity was markedly cut down. His passivity during this week was accepted by his physician, and the patient felt better because of his acceptance by a strong masculine figure. After the week, the patient became

afraid of his passive role in reference to the physician, and complained that he was being "held down" and didn't know why. In the space of two days he became suspicious of his physician, with marked paranoid distortions of all that happened in his environment. The natural course of the disease was changed for the worse in that, from the initial symptomatic improvement, the patient felt threatened by his chemically induced passivity and became overtly paranoid. The drug was stopped, his physician happened to go on vacation, and within two weeks the patient had returned to his pre-psychotic state. Psychotherapy continued, and the patient was discharged as improved after three months.

Comment: As the transference developed, he feared the passivity imposed on him by the drug since he distorted the physician's motives. He became psychotic.

5. (Case 50). M.J., aged 39, before reserpine was slow in his physical movements, gloomy, covertly hostile, sleepless, paced the floor, and showed considerable despondency. Neck movement was limited because of previous discectomy. Dose: 1 mg. p.o. for 10 days. He gained 2 lb. in 10 days. No œdema. Appetite remained fair. B.P. 130/90 went to 120/70, P. went from 100 to 70, R. remained at 16. Patient felt he was "made worse". Results on affect were considered poor. The patient became slowed, showed more psychomotor retardation and more despondency, and was gloomier. He had less ability for social contacts, and lost all ability for even subtle expression of overt hostility. He developed self-destructive nightmares, and became overtly suicidal. The major observable changes were that all symptoms of depression were increased except his pacing. The patient lay on his bed and appeared dejected. The natural course of disease was unchanged, in that a depressive reaction became sufficiently severe to be considered a psychotic depression. The patient lost his small ability for outward expression, and his long-standing somatization through headache, stiff neck, and arm pain increased. There were no side-effects. Patient returned to his pre-drug state within one week of discontinuation. He improved with about 1½ months of further psychotherapy.

Comment: In this depressed patient, the drug removed the limited ability for psychomotor activity, and the patient felt even more helpless and inadequate. A deepening of the depression to psychotic levels followed.

6. (Case 51). M.A., aged 31, before reserpine showed anxiety, restlessness, fear, inappropriate affect, bodily delusions and auditory hallucinations. Physical findings were normal. Dose was 15 mg. i.m. daily for 8 days. Patient gained 9 lb. in 8 days. No œdema. Appetite changed from poor to good. B.P. went from 170/80 to 120/70 while on drug, P. from 100 to 72, R. remained at 16. Patient felt he was "helped". The results as to affect were considered poor. The signs of anxiety, agitation and disorganized behaviour disappeared, and the patient became a quiet and resigned psychotic instead of one full of fight and turmoil and still battling with his illness. The major observable changes were that he became drowsy, lethargic, slowed down, and apparently resigned to his hallucinatory experiences. He was unable to use his previous psychotic mechanism of going through a ritual of active symbolic bodily movements to make his somatic delusions disappear. The natural course of the disease was unchanged, but an active, turbulent psychosis was changed into a quiet one. There were no side-effects. The patient was sent to another hospital where he received electroshock and insulin, but still had residual schizophrenic symptoms.

Comment: This psychotic patient was anxious and struggling with his illness. The drug removed the ability to mobilize energy into physical activity, and he became a quiet, resigned psychotic.

PRODUCTION OF PSYCHOSIS OR FURTHER PSYCHOTIC DISINTEGRATION WITH CHLORPROMAZINE

7. T.J., aged 33, before chlorpromazine showed signs of increased motor activity and speech, euphoria, flight of ideas, and a feeling that he alone was doing his job as it should be done. He had shown increasing evidence of the above for approximately one week, and had been sleepless, anxious and somewhat irritable for two or three weeks before that. He was given chlorpromazine 50 mg. i.m. q.i.d. for approximately 30 days. At the end of the second day, he was quiet, calm, and no longer overactive. He sat quietly by his bed, smiled at everyone who approached him, and when he felt "like doing something to keep busy" asked permission to wash the windows. In psychotherapeutic interviews, however, or if asked how he felt or what he thought, he stated that he could "see angels sitting in the tree tops outside the windows" and they were talking to him. He added that there was no longer a need for him to fight because all was now settled. He was waiting orders from God to join the Heavenly Father or to remain on earth awhile. He presented autistic thinking, delusions of grandeur and persecution, and ideas of reference. Thus, from an overactive person with hypomanic symptoms but no known hallucinations he was turned into a quietly hallucinated person with typical schizophrenic symptoms. He was treated over a four-month period with reality-testing psychotherapy, occupational therapy, and a therapeutic work programme. After three months he was free of delusions, hallucinations and ideas of reference. There was some residual autistic thinking.

Comment: In terms of time this was the first case in our hands to show an increased psychotic deterioration when activity, used as a major defence, was chemically removed (Sept. '54). A manic symptomatology covering a homosexual panic was changed to a quiet, but typical paranoid schizophrenia.

8. K.J.G., aged 22, before reserpine showed acting out and characterological defences (character neurosis) such as a surface affability, cheerfulness, and an apparent ease in his interpersonal relations. This latter was characterized by drive, energetic actions and much motility. Thus, he would drink beer "with the boys", boast, act "like a big shot", and spend a great deal of money to "prove" that he was a "big shot". On admission, he showed all of the above characteristics, plus marked anxiety, fear that he was going insane, loss of appetite, pain in the right genito-femoral region, and, beneath his motor activity, a feeling of sadness and despondency. Because of his marked anxiety, he was given chlorpromazine 50 mg. i.m. t.i.d. for one day, then 50 mg. p.o. t.i.d. This resulted in a marked diminution of the patient's motor activity. He felt tired and weak, and complained of having "a dry mouth" and of being dizzy. He was unable to engage in his usual motor activities such as sports, and spent much time lying in bed. With this physical inactivity, he became more overtly sad, despondent, and irritable; at night time, he began to hear voices, which frightened him, although in the morning he was uncertain as to their reality. The drug was discontinued when the above phenomenon developed after six days. He became more active one day after the drug was discontinued, and within the next three days, with return of his motor outlet, much of the depressive element lessened, although he remained markedly anxious. He was transferred to another hospital because of ineligibility for treatment under D.V.A.

Comment: Here again removal of activity, which was a major defence and "demonstration of his masculinity", resulted in further psychic deterioration in a patient with a borderline state.

9. (Courtesy of Dr. C. Conway Smith—Montreal.) This 74-year-old man had had a previous manic episode 15 years ago, which had been treated by E.C.T. This

latter had not interfered with his usual outgoingness, at the time.

In September 1955, he consulted a physician because of increased irritability, impulsiveness, and the beginnings of increased motor activity. Normally this patient was an extremely active, exacting, and aggressive business man whose sensorium and intellectual capacities were unimpaired, and who was considered to have an obsessive-compulsive personality with a tendency to marked mood swings. Because of increased symptoms his physician put him on an unknown dose of chlorpromazine. This dose was sufficient to markedly cut down his activity, and with the removal of this outlet the patient became increasingly disturbed. His irritability increased and the patient felt inwardly more excited, even though he was unable to express this at a motor level. The patient developed jaundice at this point, and an exploratory laparotomy was performed. Being thus further immobilized, he became even more excited and difficult to manage. A psychiatrist (Dr. C. C. Smith) was consulted at this point, and hospitalized the patient in a closed setting. Reserpine 1 mg. b.i.d. was substituted for the chlorpromazine. The patient became more mobile and physically active, since the dose of reserpine was insufficient to have the same chemically holding effect that the dose of chlorpromazine had had. As the patient became more physically active, his agitation and excitement diminished. He was given ground privileges shortly after his arrival at the closed hospital, and improved markedly over a period of one to two months. Towards the end of his hospital stay, some peripheral œdema was noted and reserpine was discontinued. Dr. Smith felt that the use of reserpine in sufficiently low dosage to permit the patient recourse to activity as a defence helped him cope with his fear of being made helpless, and thereby less manly.

Comment: Here again, removal of the patient's long-established mode of reassuring himself as to his adequacy and manhood through activity produced further psychotic deterioration. Restoration of activity helped his recovery by offering an old and well-established pattern of expression.

ENHANCED ANXIETY PRODUCED BY RESERPINE

10. (Case 9). S.J., aged 25, before reserpine showed marked anxiety, poor control over aggression, weakness in the knees and tremor of the hands and legs when angry. He often became panicky, and had a slow slurred speech. He had from his early childhood been awkward, and showed a marked inability to master muscular co-ordination. He had spontaneous hypoglycæmia with fugues. He hyperventilated when he was panicky, and at times had hypnagogic hallucinations. He was an asthenic, thin man, with a marked awkwardness which seemed to express his inability to master himself. Dose: 4 mg. orally daily for 8 days. The patient gained 5 lb. in 7 days. There was no œdema. His appetite remained good. His B.P., P. and R. went from 120/76, 72, and 20 before the drug to 120/70-90/68, 68 and 22 while on the drug. The patient felt he was "made worse". The results on affect were considered poor. The patient was made weak and dizzy, and his already intolerable awkwardness increased. He felt more helpless and passive, looked worse and felt worse. The major observable changes were weakness, tiredness, dizziness, increased awkwardness, and enforced passivity. The result on the natural course of the disease was unchanged, but the patient felt infinitely more anxious and less the master of himself. Side-effects were headache and nasal stuffiness. Investigation showed involvement of total body and psyche in the illness (i.e. autonomic nervous system, endocrine, psychic, muscular and E.E.G. findings). Reserpine was stopped and mild phenobarbital sedation substituted. Psychotherapy continued, and the patient felt considerable relief within three days (as the drug wore off). He improved under psychotherapy and was discharged 10 weeks later.

Comment: The drug increased his already intolerable awkwardness by removing his capacity for voluntary energetic movement. This made him feel less adequate, i.e., less manly, and increased his anxiety.

11. (Case 17). J.C.A., aged 39, before reserpine had somatic pains (low back pain, pain in right shoulder blade and right knee). He was unhappy and moderately despondent. He was irritable, hostile, and aggressive and insisted that the pain was organic in origin. Chronic prostatitis, an enlarged prostate and moderate essential hypertension (150/100 mm. Hg) were found on physical examination. Dose: 2 mg. orally for 5 days. His weight did not change and his appetite remained good. His B.P., P. and R. went from 150/100, 80, 20 to 100/70, 72, 20. The patient felt he was "made worse". The results as to affect were considered poor. The patient was made weak, dizzy and more passive. He reacted to this by increased anxiety and agitation. He felt useless, frightened, and weak, and his pains increased. The major observable changes were weakness, dizziness, agitation, and more passivity. The result on the natural course of the illness was unchanged. The patient remained an obsessive-compulsive with somatic symptoms and a marked dependency as manifested in his desire for a pension. Side-effects were diarrhœa for 24 hours and a stuffy nose. The drug was stopped, and he lost his fear of the effects of the drug in two to three days, and along with this the feelings of indecisiveness and frustration. He continued on psychotherapy. His depression was significantly improved through working with his hostility. In the next two months his somatic complaints and his demands for pension persisted.

Comment: The physiological effects of the drug threatened this passive-dependent man by reducing his capacity to control his own body. He interpreted this as a "demasculinization" of himself and became markedly anxious, with increased somatic complaints.

12. (Case 28). C.J., aged 29, was weepy, unhappy, covertly hostile and manipulating in his interpersonal relations. He was effeminate in gesture and speech. He had headache and nausea, and seemed to be a very passive and dependent person. Physical findings were normal. Dose: He received 2.5 mg. i.m. the first day and responded with marked anxiety and more weeping, all directed at the nursing staff in an attempt to manipulate them into stopping the injections. On the second day he received 5 mg. i.m. and felt so terrible, with such marked panic at night, that the medication was cancelled. He stated that he could not stand the weak, helpless feeling the drug gave him, and that the thought of it made him sweat and shiver. The patient felt he was "made worse". The results as to affect were poor. His headache, sadness and anxiety were worse, and on the second evening he had a mild attack of panic. The major observable change was a marked increase in his anxiety to the level of panic. Nausea was the only side-effect, after withdrawal of reserpine. Psychotherapy plus the hospital milieu helped the patient. He left, improved, approximately one month later.

Comment: Here a passive dependent, somewhat effeminate man with considerable anxiety and a mild depressive reaction, panicked at the chemical effects of being made weaker and less active by the injections. He resorted to his characterological defence of manipulating the environment away from a "dangerous" situation.

13. (Case 37). Miss W.P., aged 21, before reserpine was intensely anxious, fearful, unhappy and impulsive. She was physically very active, and blinked her eyes continually. She had suicidal thoughts, and was very disturbed by her conscious awareness of being attracted to other women. Physical findings were normal. She received 5 mg. orally daily for 15 days. She gained 10 lb. in 15 days. There was no œdema and her appetite remained good. Her B.P., P. and R. went from 120/70,

68, 16 to 95/50, 72, 16 in 48 hours. B.P. stabilized at 110/60. She felt she was "made worse". The results as to affect were considered poor. The patient became "groggy", weak, dizzy and felt chemically held down. She was very frightened by this. She lay on the bed, slept continually except at meal time, and was very irritable and hostile. She began refusing the drug. The natural course of the illness was unchanged. There were no side-effects. The drug was discontinued, and she reverted to her pre-drug state with much relief. Psychotherapy continued, and she improved to a limited degree in the next three months.

Comment: This girl had a marked attachment to the treating physician, and interpreted the drug as a seduction or assault by him. The physiological effects in making her weak, tired and relatively helpless were doubly threatening because they removed her ability for aggressive independent action as well.

14. (Case 53). C.M., aged 37, before reserpine was sleepless and moderately anxious, with an obsessive-compulsive personality, and a right-sided spasmodic torticollis of 18 months' duration. He received 5 mg. i.m. daily for 10 days, then 3 mg. orally for 10 days. He gained 3 lb. in 20 days, his appetite went from fair to good and there was no œdema. B.P., P. and R. went from 124/84, 80 and 20 to 110/70, 72 and 20. The patient felt he was "not helped". The results on affect were considered poor. He was slowed, felt "lifeless, doped", "useless", had a sad facies, and looked dull and inert. He showed a marked diminution in his social activities. The natural course of the disease was unchanged. He became more depressed and anxious and discharged himself from hospital.

Comment: The patient became more depressed and anxious, feeling threatened at being chemically held down. He considered this as an assault and a seduction, and ran away from it by discharging himself from the hospital.

Two other cases with reserpine will now be presented with the same psychodynamic and physiological constellations. Here however, in contradistinction to the other cases, circumstances were such that they were benefited by the drug.

15. (Case 26). C.J., aged 29, had been hospitalized for several months with some benefit. He went on a week-end pass and spent much of his time drinking beer with male friends. He panicked afterwards, and made a suicidal gesture by swallowing some barbiturates. He returned to the ward despondent, very anxious and almost in panic. He was jittery, perspiring, trembling, crying. He was given 2 mg. i.m. as night-time sedation, and he received the same dose nightly for seven days. The patient felt that he was "helped". Results as to affect were considered good. The patient was initially anxious and afraid of going to sleep. He remained awake most of the first two nights. When he was told that he was in a hospital, that his fear of what could happen to him was understood, but that nothing was going to happen to him here, he relaxed and calmed down, and at the end of the seventh day asked for further injections.

Comment: This patient had been in homosexual panic, i.e. he feared that an unconscious uncontrollable urge for some sort of homosexual contact would become conscious. He thus feared a drug that would render him more helpless. But in the "safe" reassuring atmosphere of the hospital, he relaxed and obtained unconscious but safe gratification of his need to be assaulted (i.e. injections) and felt better as a result. The safe hospital milieu and understanding physician made the difference between a good and bad therapeutic result in this case.

16. (Case 47). W.Y., aged 38, before reserpine was so angry at being jilted by a girl that he had been on a five-day binge and was shaking, sweating, pacing the floor, crying and expressing great fear of suicide or homicide. He was known to have a violent temper that was difficult to provoke, but once provoked he had in the past been known to give way to great physical violence. Physical findings included slight jaundice, a large tender liver and early bronchopneumonia. The diagnosis was acute depression with alcoholism, infectious hepatitis and bronchopneumonia. The patient received 40 mg. reserpine daily orally and i.m. for 20 days, and felt that he was "helped". The results on affect were good. Anxiety and tremor were dispelled; the patient was inert and listless in bed and was therefore passive, and reassurable as to violence. On psychotherapy and medical treatment he moved towards aggression related to reality. He was slowed to the level of complete bed rest for one week, after which he was able to move, but moved like an automaton. The natural course of the disease was changed. The drug interrupted an acute psychotic episode by rendering impossible the threatened eruption of aggressive feelings and drives. Nasal stuffiness was the only side-effect. He returned to army duty mildly euphoric after reserpine was stopped.

Comment: Here the very passivity and helplessness, which in other circumstances this man would have probably feared as a feminizing thing, were welcomed and sought as protection against his aggressive impulses—with good therapeutic result.

DISCUSSION

A series of patients have been presented in whom two drugs, quite useful in psychiatry and enjoying a current vogue, caused a psychotic process, further deterioration of a psychotic process, or enhanced anxiety. Both these agents have fairly standard physiological effects for a given dose. In psychiatry, these physiological effects are useful to relieve selected are symptoms. The drugs are therefore not psychiatric "specific agents" but *symptomatic* drugs.

A standard physiological effect of both drugs is to chemically "hold down" the patient. It makes him feel tired, weak, and, in adequate dosage, incapable of mobilizing much energy into physical activity. There are other effects which are predominantly *psychological* and are the result of the way in which the physiological effects fit into the patient's way of handling and expressing his conflicts (i.e. defences). When a patient does badly, it is due to the way in which the physiological effect *psychologically* threatens him.[10]

This report does not mean to imply that reserpine and chlorpromazine have no place in psychiatry. Rather, the good or bad effect depends on the last-mentioned consideration. In all the cases reported here, the desired physiological effect for which the drug had been given was reached. That is to say, the patient had been slowed, felt tired, was calmed, and had his

activity cut, and it was precisely this physiological effect that was *psychologically* threatening to the patient.

The following common psychodynamic elements were found:

1. *Fear of increased passivity.*—The chemical "holding down" action of these drugs removed activity as an outlet. A large group of patients with marked doubts about their masculinity, and with marked feminine identifications, express these in conflicts over their sexual, social, and intellectual potency. Many of these patients use activity in one or all of the above spheres as a means of reassuring themselves that they are adequate males. When this activity is used as a *major* defence, removing it chemically, by rendering them incapable of energetic action, is very threatening. These patients consider activity to mean masculinity and passivity to mean femininity (Cases 1, 2, 3, 6 and 7 show this feature).

Thus for the same intrapsychic conflict, a better integrated defence, i.e. one allowing better contact with reality (activity), was chemically removed. Under the threat of increased relative passivity (femininity) these patients reacted with more poorly integrated defences, because of the intolerable anxiety produced (see Dr. D. G. Wright's theory of schizophrenia[13]). This results in either enhanced anxiety or further breaks with reality (i.e. psychosis).

2. *Fear of impaired body function or of body image changes.*—Another group showed essentially the same psychodynamic conflicts over psycho-sexual identifications as group 1 but expressed it clinically as fear of impaired body functioning or of body-image changes. This group interpreted the physiological effects of these drugs, and/or the multiple side-effects, as a lessening or impairment of body function. Again, as in group 1, and for the same psychological reasons, changes meant increased passivity (i.e. femininity). This lessened control over themselves caused increased anxiety, and if the latter proved intolerable, a "downward" rearrangement of the defences into psychosis. Patients with obsessive ruminations over bodily health often show increased anxiety when the multiple physiological effects and side-effects of these drugs increase somatic dysfunctioning.

3. *Increase in depression.*—The depressed patients became more depressed. The action of these drugs in further limiting the expression of hostility through psychomotor activity, or limiting ability for some interpersonal relations, increased the feeling of personal helplessness and unworthiness, and therefore unconscious aggression as well.

4. *Interpretation as assault or seduction.*—Several patients, including the only woman in this report, interpreted the physiological effects, in rendering them less active, weak, passive and less the master over themselves (i.e. more in the doctor's power), as an actual or threatened assault or seduction. This they interpreted as either homosexual or heterosexual. When this was too threatening, and therefore unwelcome, the psychiatric disability increased. It should be pointed out that safe unconscious gratification in the protective hospital milieu, of the same need to be seduced or assaulted can prove beneficial (cf. Case 15).

From the above, it becomes clear that the clinical nosological entity produced—e.g. paranoid reaction, enhanced anxiety, depression, or agitation—is not dependent on a specific action of the drug concerned, but is rather a result of the way in which the patient responds, with all his total assets, to the removal of one of his important defences, such as activity. Whether a depression or a paranoid psychosis is produced is the result of the interplay of many forces, the constellation of which has a high degree of individual variation for any particular person. This can only be evaluated by careful individual psychodynamic study.

We therefore believe that any variety of psychiatric condition is possible, depending on the interaction of the physiological effects of these drugs, the psychological effect of this on the very complex defences, and the reality situation. It is naive to attribute these effects to some possible vague specific action of these agents on the brainstem,[6, 7] since the physiological effects of these drugs are fairly constant for any one dose and were also present in patients who did well on these agents. As another example of this, Case 16 shows a good result, i.e. beneficial to the patient, from the physiological effects in holding this man down, because he feared eruption of his aggressive feelings. It is probable that the same man would have been threatened instead of supported in other circumstances than these, because of his fear of passivity.

SUMMARY

A study of 14 cases of psychotic reactions, further psychotic deterioration or enhanced anxiety, produced with reserpine and chlorpromazine, is presented. Two other examples of the same psychodynamic elements, with benefit, are presented in contrast. We believe this to be the first work to deal specifically with psychiatric cases and offer explanations for this phenomenon.

All these cases had common psychodynamic elements.

The physiological effects of the drugs were fairly constant for a given dosage and were present both in those patients who reacted badly and in those who did well on these agents.

It is felt that these untoward reactions had nothing to do with the physiological effects *per se*, but rather with the way in which the physiological effects *psychologically* threatened the patient.

The psychological reaction produced was nonspecific as regards the drug but specific as regards interaction between the physiological effects and the particular psychic, interpersonal, and reality factors in the patient concerned. Thus any variety of psychiatric nosological entity is theoretically possible.

This paper presents some psychodynamic criteria from which clues as to the proper selection of cases have been deduced.[10]

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G. J. SARWER-FONER:
4631 Sherbrooke St. W.,
Montreal, Que.

W. OGLE:
Pinel Foundation Hospital,
Seattle, Washington.

RÉSUMÉ

Les auteurs présentent une étude de 14 cas de réactions se rapportant à la psychose, de détérioration psychique augmentée ou d'angoisse accrue, produites par la réserpine et le chlorpromazine. En contraste, ils présentent deux autres exemples des mêmes éléments psychodynamiques qui ont bénéficié du traitement. Les auteurs croient que leur étude est la première à traiter spécifiquement des cas des psychiatrie et à offrir des explications de ce phénomène.

Tous ces cas présentaient des éléments psychodynamiques communs (voir le texte).

Les effets physiologiques de ces médicaments furent assez constants pour un dosage donné et se rencontrèrent chez les malades qui réagirent mal et chez ceux qui bénéficièrent des médicaments.

On suppose que ces réactions fâcheuses n'avaient rien à voir avec les effets physiologiques per se, mais plutôt se reliaient à la manière dont les effets physiologiques menaçaient le malade *psychologiquement*.

La réaction psychologique produite ne fut pas spécifique au médicament, mais le fut à l'action réciproque des effets physiologiques d'une part, et des facteurs particuliers psychiques et personnels et de la réalité concrète propres au malade concerné d'autre part. Ainsi, n'importe laquelle variété de maladie mentale est théoriquement possible.

Ce travail présente quelques critères psychodynamiques desquels on a déduit des indices servant à identifier correctement les cas. M.R.D.

"COIN" LESIONS OF THE LUNG

There are as many definitions of the term "coin" lesions of lung as there are reports in the literature. Some writers state that a "coin" lesion has no size limitation, and that this terminology may be used if the lesion is well circumscribed. Others state that a limitation of size is necessary. In the current investigation, 124 such lesions were studied, and the criteria for inclusion in the series were: (1) diameter between 1 and 4 cm.; (2) well-circumscribed tumour; (3) lesion surrounded by lung; (4) no evidence of major bronchial obstruction.

In the previous literature, 729 such lesions have been reported, and 262 (37.31%) of this group were malignant. Among 124 "coin" lesions reported in the present study, a much higher cancer incidence was found (52.4%). Malignancy was much commoner in lesions in patients over 40 years of age—a very important point, deserving of considerable emphasis. Most "coin" lesions do not cause symptoms; an accurate diagnosis can be made by clinical and laboratory procedures in *less than one-quarter of all cases.*

Since exploratory thoracotomy is no longer considered a "dangerous operation", it is recommended as a diagnostic procedure when other measures fail to provide a convincing definition of a particular "coin" lesion.—W. B. Ford *et al.*: *Am. Rev. Tuberc.*, 73: 134, 1956.

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THE FUTURE OF THE DEAF CHILD*

R. W. FANJOY, M.D., C.M., *Montreal*

MANY PERPLEXING and worrisome problems confront the parents who are told "Your child is deaf"; my wife and I were no exceptions. The apprehension, fears and sorrow for the child's future at first seem insurmountable; however, we now know that with modern therapy a deaf child may become a useful and well-adjusted citizen.

A deaf child has been variously defined. At one extreme we find any child without his full power of hearing considered deaf; at the other extreme many workers say that a child must have complete loss of hearing to be called deaf. In this article, a deaf child will be taken to mean "any child who cannot be successful with his sense of hearing, even with a hearing aid alone; he must have, in addition, special therapy so that he may develop speech and understand ordinary conversation." We will not concern ourselves with the hard-of-hearing child whose hearing, although defective, is sufficient for him to learn to talk and adjust himself to his surroundings.

A deaf child is usually brought to the doctor because of lack of speech. When the parents are told that this speech-handicapped child is deaf, many questions arise which they want answered. These questions are real worries which may be reflected in the handling and training of this deaf child and in many cases can be detrimental to the successful rehabilitation of their son or daughter. All these questions can be summarized in one thought, "What is the future of my deaf child?" It should be the duty of the doctor to answer them as fully as possible and thus calm the fears and visual imaginations of the parents. In other words, it is not sufficient to diagnose the case only; the doctor must also advise the parents of the need for family training for the child and direct his attendance in a specially equipped school for the deaf. Family training is of the utmost importance, and in order that it may be of the highest efficiency the parents must be put at ease. They should be assured that, provided the child receives the necessary training early, he will be able to communicate well with the public.

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In a typical case, a three-year-old child is brought to the doctor because he is not talking. The child was born after a full-term pregnancy with a short and uneventful delivery; following delivery, the baby breathed and cried well; he had no feeding problems or illnesses. The various milestones of development were passed at the normal average ages, except that speech was retarded. The child vocalizes noisily in a flat and monotonous tone to attract his parents' attention or to express fear, anger, discomfort or joy; this vocalization cannot be distinguished as words, so cannot be called speech. His play is usually quiet; he does not hum or sing to himself, neither does he "chug-chug" like a train or roar like a motor car when playing with toys; he shows no preference for noisy toys. He expresses his wants and feelings by a series of gestures and pantomimes. The parents state that the child is nervous and restless because he is constantly on the move. "Why, Doctor, he can't sit still a minute." On closer questioning, we may find that these movements are designed to keep moving objects or shadows in his field of vision. His laugh is less frequent and spontaneous but louder than the laugh of a child with normal hearing. He is friendly with others but sometimes has a temper tantrum when he fails to make himself understood. His behaviour is constant from day to day. The family history shows no deafness in his two younger brothers or in past generations. Prenatal history reveals one significant factor—the mother developed measles in her second month of pregnancy.

Examination of the child reveals little or no response to speech; he walks with a shuffling gait; otherwise the examination is essentially negative. Results of intelligence tests are slightly below the normal limits. Psychiatric examination reveals no adverse conditions in the child's background or life. Encephalogram and neurological examination show no abnormality of the central nervous system.

Hearing tests, using calibrated toys and noisemakers, elicit little or no response in either ear. When the toy or noisemaker is brought forward into the field of vision or casts a shadow within the child's sight, he immediately turns in the direction of the operator; he may grasp the toy but does not attempt to reproduce the sounds.

A review of the complete clinical data establishes the diagnosis of deafness, probably due to the mother's measles early in pregnancy. It also

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rules out other conditions simulating deafness such as brain injury, mental retardation, and psychological disturbance. The parents are now told, "Your child is deaf." Possibly they have been conscious of this previously, but inwardly had a faint hope that all would be well. Now their last hope falls like a leaf in the wind. Immediately these hopes are replaced by questions either expressed or left unsaid, which they need answered to relieve their worry about the child. I will now attempt to present a few of these many questions and to illustrate how they may be answered for the parents.

1. *Will My Child Ever Talk?*—Yes, your child will probably learn to talk provided he receives special training early. By talk, I mean he will be able to communicate with others socially. A child with normal hearing learns to talk by constantly hearing and repeating sounds presented to him; in the same way a deaf child learns to talk by repeatedly seeing other persons speak clearly and distinctly. In the family circle as well as in special schools for the deaf he first learns to be attentive to the speaker; he must watch the speaker's face when trying to communicate. Just as a hearing child, sooner or later, begins to associate a certain sound with a definite object, action or vision, so will a deaf child begin to associate certain movements of the lips and face muscles with the same objects, actions or visions. Thus your child begins to lip-read. Gradually, although he cannot hear, he improves his lip-reading and adds new words to his extra-auricular "hearing". In this way he broadens his scope to interpret speech from others. As a continuation of repeatedly hearing sounds, the child with normal hearing gradually acquires speech; likewise a deaf child acquires speech through repeatedly seeing speech presented to him; he is slower in learning speech than a child with normal hearing because he must rely on tactile and visual therapy. By seeing the movements of the speaker's face and feeling the vibrations in the speaker's throat, he learns to copy the movements necessary for the production of sounds and words. In this way he learns to speak satisfactorily to others. His speech will not be the same as that of a hearing child but it will be intelligible. A child with normal hearing will learn to modify his voice according to his surroundings, and by repeatedly listening he learns to modify his voice for emphasis and inflection. In the deaf child this normal stimulus to follow speech of his own society is lost. As a result a deaf child's voice will tend to be flat and toneless. The speech, although defective, will meet his need for communication in society. Many of these children acquire speech that can be understood easily by the general public; in fact, many teachers in our schools for the deaf are graduates from a class of deaf children in the same school or others. A few children acquire speech of a poorer quality, but this is sufficient for understanding by friends, relatives and others accustomed to hearing them talk. A minority of deaf children will acquire a means of communication without speech. The majority of the last group are children whose training was neglected during the pre-school age or who have other handicaps along with the deafness.

2. *Will My Child Ever Hear?*—No training will improve your deaf child's hearing, but through training he will learn to use residual hearing, if any, to better advantage. By lip-reading his speech discrimination tests will improve so long as he can see the speaker. That is, repeated hearing tests of your child will never show improvement of hearing but his ability to discriminate between the various speech sounds will improve in subsequent tests. You may have seen a child who lost a leg in an accident; at that time you think of the dreadful deformity which the child sustained. Finally you see the same child fitted with an artificial limb and playing happily with his mates; he now has no handicap except a slight limp. You now accept the loss of the leg and thank God that he can take his place in society without using a wheelchair. The same will be true of your deaf child; you now feel keenly his loss of hearing but after a period of training you too will thank God that he has been fitted with an artificial method of hearing and that he now can communicate with his friends, relatives and associates.

3. *Could Nervousness Be the Reason Why My Child Does Not Talk?*—Two mothers have been heard to raise this question, and it was difficult to convince them that their children should be sent to a school for the deaf. In one case the mother stated later that her rejection was because "Auntie" knew a very nervous child who did not talk until the age of six. A nervous child may not talk and may thus be similar to a deaf child but the two are not identical; their behaviour patterns are different. A nervous child may be restless and continually moving about but the

movements are haphazard and serve no definite purpose. In the deaf child these movements serve a definite purpose. The deaf child lacks hearing and so depends on his visual, vibratory and other senses for information from the outside world; the most important of these senses is sight. Sight, unlike hearing, is limited to only a small field of vision in front of the child, and any object in his field of vision hides the more distant sight; because of this your child must be continually on the move so as to keep himself in contact with his environment. A deaf child compensates for his loss of hearing by a greater awareness of the other senses; this does not mean that your child's sight, for example, is better than that of a child with normal hearing but he uses his sight to a better advantage; he, therefore, becomes more aware of movements and objects within his field of vision. Sight is his main avenue of contact with the environment.

4. *Can My Child Be Fitted With a Hearing Aid?*—Your child may benefit from a hearing aid but not until he has received preliminary training. Most parents think that if their deaf child can be given a hearing aid he will learn to talk by himself. This is indeed wishful thinking. Whether any deaf child can be fitted with a hearing aid depends upon the type and degree of his hearing loss and upon the individual himself. Every case must be considered individually; the final decision whether your child is suitable for a hearing aid will be the trial of using it. A hard-of-hearing child will be served well with a hearing aid alone; the sounds can be amplified easily to his speech discrimination level so as to render conversational speech intelligible: the necessary amplification is not sufficient to cause pain or discomfort in his ear. A deaf child, on the other hand, requires a much greater amplification to render speech intelligible; the sound, so intensified, entering the ear causes discomfort or pain. The amplification, therefore, must be reduced to a level that is comfortable to the ear; this reduction of intensity is at the expense of intelligibility for speech. Thus, the child hears some sounds clearly, but in between are gaps which are not intelligible. The child must be taught to fill in these gaps by lip-reading so as to understand whole words and sentences. This is why your child must receive special training even though he wears a hearing aid. Finally, a totally deaf child has no residual hearing; therefore, no amplification will allow him to hear sounds. However, a totally deaf child is very rare; the ordinary hearing tests may show no response but there is still possibly some vestige of hearing which cannot be detected by our present-day equipment. Even if your child were in this group, he might profit from a hearing aid at a later date. No deaf child will learn to talk satisfactorily by using a hearing aid alone; he must have special auditory training both before and after being fitted with a hearing aid.

5. *If We Have Another Baby, Will He Also Be Deaf?*—Many parents raise this question, particularly if it is the first child who is deaf. To answer this question we must consider each case individually; I will present a few guiding factors for answering in each individual case.

Deafness may be divided into two groups: *Congenital Deafness*—that is, deafness which is hereditary and may be passed on from one generation to another. Thus we would expect to find a history of childhood deafness in the mother, father or other ancestors. If this were the case, there is a stronger possibility of your next child being deaf; however, he will not necessarily be deaf. This possibility is increased if the deafness is on both your maternal and paternal sides of the family.

Acquired Deafness—that is, deafness which is due to some factor in prenatal, natal or postnatal life which has acted upon this child to produce deafness. If this factor is permanently present to act upon succeeding babies, the chances are that each baby will be deaf. As a rule, this factor is present only with this one pregnancy; the remaining pregnancies will be free. Thus, if your child's deafness is congenital, future babies *may* also be deaf; if the deafness is acquired, your future babies will probably have normal hearing.

6. *How Should I Handle My Deaf Child?*—The ultimate goal for training of any child, either deaf or with normal hearing, is to fit him into our society. There are three guiding principles which will help you in the handling of your deaf child. These principles, if followed, will lead you to the goal:

(i) You must give your child every opportunity to repeatedly see words, phrases and sentences presented to him, so that he may be initiated into lip-reading. The home provides an ideal place for this training. Everyday duties afford ample opportunity for correlation of actions with appropriate words or sentences,

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such as "put on your cap", "eat your dinner", "go out to play", or "good-night". If your deaf child is repeatedly told to do these things, he will soon learn by lip-reading what you want him to do. Thus, take every opportunity of talking face to face with your child as soon as you suspect or know he is deaf; this will make him aware of communication and will also develop his ability to lip-read. If he has not yet started attending a school for the deaf, it will give him a start for future education; if he is already attending a school for the deaf, it will supplement his school training.

(ii) You must treat your child as a normal child and give him the same attention, personal contacts and companionship as you would a child with normal hearing. A normal child is first a member of the family circle; he later joins with friends of his community; at the age of six years he joins the church and school societies. After graduating from high school he broadens out into a professional and business society. During all these steps he is gradually moulding his own character and behaviour to fit himself into each new society. He knows well that society will not change to meet his demands but that he, himself, must change to meet society. It is the same way with a deaf child; he, too, will graduate from high school and seek some occupation or profession. He must fit himself into a new society; this society, unlike himself, consists mainly of persons with normal hearing. Therefore, his training must include companionship with children of normal hearing; he must be encouraged to play and associate with others so that he can gradually mould himself into each new society. During the Dark Ages it was customary to shelter the deaf child within the home and to consider him as a mentally deficient child; he was never allowed to go out and associate with other children and society. Even today, we find many parents doing the same with their deaf child. You must come out of the Dark Ages and into a more modern age if you wish to rehabilitate your deaf child successfully.

(iii) You should limit the use of signs and sign language. Any signs or gestures should be accompanied by words and all sign language gradually lessened so that the child will become more dependent on lip-reading. Sign language, if once established, is difficult to break down, and the child also loses his initiative for verbal communication. You must encourage your child to develop a method of communication which is understood by the general public; sign language is limited in its use, as only a few persons can use and understand it.

To these three principles may be added two general suggestions for the training of your deaf child. Although these apply equally to any child, whether hearing or deaf, they are frequently neglected in the deaf child because of his handicap. (a) Do not cater to or always give in to your child. In any family there is a tendency to either reject or cater to the deaf child; between these two extremes lies the happy medium. Within the family circle there is a greater tendency to do everything for the child and to submit to all his wants and requests. If this continues he will become dependent on others, so that when he leaves the family circle he will still expect his associates to attend to his needs and to submit to all his whims and fancies. You must encourage your child to build a feeling of independence for himself and not to be dependent on others. (b) You must explain to your child what you want him to do. Most of the temper tantrums and behaviour problems of the deaf child arise because he does not understand what you want. If you only take the time and patience to explain to your child just what is expected of him, he will co-operate much better. It will be difficult to do this with your deaf child, but by using talk and gestures he will soon learn to know your wants.

When the parents are told that their child must be sent to a school for the deaf further questions arise:

7. *Why Can't We Wait Until My Child is 8 or 9 Years Old?*—It is now recognized that the training of a deaf child should begin as early as possible. His pre-school education is of the utmost importance in his development of speech and language. A child with normal hearing learns to discriminate between sounds and to reproduce these sounds during his first three years of life. The reproduction of speech depends upon the memory of these sounds. As the child becomes older his memory becomes progressively less for new sounds. In the same way the deaf child learns to talk by remembering certain face and lip movements; his memory for these movements also becomes progressively less as he grows older. The training of your deaf child is a long and arduous task; the sooner this training is

started, the greater are the chances that he will acquire good speech and become a well-adjusted child.

8. *How Long Will My Child Attend a School for the Deaf?*—The length of time necessary for the training of your child will depend upon the individual child himself. The handicap of deafness slows the educational progress of a deaf child in comparison with a child of normal hearing. If early and adequate pre-school training is given, your child should have a good basis for language and speech by six years of age; his education in the regular school subjects can then begin, but he will continue speech and language development as in the pre-school age. By 17 or 18 years of age he should have completed his high-school education and he will then be ready for vocational training in preparation for his future work or profession. Many deaf children will be able to successfully enter a regular school with children of normal hearing some time during their elementary or high school years.

The above discussions have been related to a deaf child with no other handicap. It must be remembered that many deaf children also have further handicaps which must modify their future training and prognosis. These accompanying handicaps may be mental retardation, brain injury or a neurotic personality. In cases with multiple handicaps, the child must first be treated according to his major handicap. If a child's major problem is mental retardation with an accompanying problem of deafness, it will be useless to attempt his education in a school for the deaf. He is just not mentally able to absorb and retain the knowledge necessary for lip-reading and development of speech; he must be trained in a school for mentally retarded children. Similarly, a child whose major problem is brain injury or a neurotic personality with an accompanying deafness will not be successful in a school for the deaf. However, if deafness is the child's major handicap and he is only slightly mentally retarded or brain injured, he will be trained best in a school for the deaf. The prognosis in cases of multiple handicaps is worsened according to the degree of the second handicap. The mentally retarded, the brain injured and the neurotic child may lack speech, but are not necessarily deaf.

Another handicap which complicates the training of a deaf child is blindness. A child who is deaf and also blind cannot learn lip-reading because of loss of sight. His case, however, is not hopeless, as it may seem at first thought. He can be taught to use his tactile and vibratory senses as his means of contact with the outside world. His is a very long and arduous course, but in the end he too will become successfully rehabilitated and develop a satisfactory method of communication.

The future of the deaf child is also greatly influenced by the public attitude towards him. The so-called friendly public frequently increases the problems of a deaf child and his parents; this is often due to ignorance concerning what can be done for a deaf child or how the deaf child can be helped by education. It has often been said that the education of a deaf child should be supplemented by a correspondence course for all his friends and associates so that they would understand him better. If this were possible, the progress of the deaf child would be greatly increased. Within the past few years the following has been said to the parent of a deaf child: "I suppose you will send him to a school for the deaf to learn sign language; you will have to get a book and study sign language yourself." "You will certainly have a burden on your hands for the rest of your life; he will never be able to do anything." "Your child is deaf and dumb; my sympathy goes out to you since you will never hear him speak." These absolutely false statements reflect the attitude of the greater portion of the public towards a deaf child. All this is disheartening and frustrating to the parents and tends to discourage further training of their child.

The deaf child is usually sensitive about his handicap, and anything which attracts his attention to his deafness aggravates this sensitiveness. The lack of understanding by the general public of this personality trait can greatly impair the child's adjustment to his environment. When we, as persons with normal hearing, have difficulty in expressing ourselves to a a deaf associate we usually raise our voice. This increased loudness has two detrimental results: (1) it attracts other people's attention to the child, and makes him more aware of his handicap so that he tends to withdraw from society; (2) because of our raised voices we are no longer talking normally; our lip and face movements are made more difficult to read. Thus the child has now a greater difficulty in understanding our conversation than if we had talked normally and used the move-

ments which the child is accustomed to reading. If we wish to help a deaf child to understand, we must talk clearly, normally and distinctly; this is much more effective than shouting.

The future of the deaf child is dependent on the combined efforts of the home, school, general public and doctor; to this should be added the individual himself. It could be said that the four cardinal virtues in the training of a deaf child are faith, hope, understanding and guidance.

1. *Faith, as displayed by the parents*: that they may have the greatest confidence in their doctor and his guidance so that unnecessary expense and valuable time may be saved, instead of travelling from one doctor's office to another in the hope that some medical or surgical treatment may help their child. The parents must have faith in the school so that regular and early attendance may be encouraged. Lastly, they must have faith in their child and know that he, through special training, will ultimately take his place in the world as a useful and well-adjusted citizen.

2. *Hope, as held by the school:* that it will have the fullest co-operation of the parents in the teaching of the deaf child; that the parents will enter whole-heartedly into the parent-teacher association for the understanding of all the child's problems and learn how they can help the child's training at home in keeping with the school's methods of education.

3. *Understanding, as needed by the public:* that they may understand the deaf child's problems and do all they can to help him overcome the handicap and at the same time do nothing that would be detrimental to the child's success.

4. *Guidance, as the duty of the doctor:* that he may conscientiously and diligently direct the parents concerning the necessities of their child's education, and do all he can to overcome the many obstacles in the minds of the parents to the successful rehabilitation of the child.

All four virtues are necessary; if any one virtue is lacking the child will not become a competent member of society.

THE GOFMAN INDICES IN CORONARY ATHEROSCLEROSIS*

J. C. PATERSON, M.D.,
BETTY R. CORNISH, B.Sc. and
E. C. ARMSTRONG, M.D., C.M.,
London, Ont.

IN A SERIES OF PUBLICATIONS beginning in 1950,[1] Gofman has claimed that a measurement of the serum lipoproteins provides a way to forecast the likelihood of human subjects' developing coronary artery disease. The measurement is said to apply even in the absence of clinically overt findings and long before the subjects actually develop clinical evidence of the disease.

The lipoproteins incriminated originally by Gofman were those in the Sf 12-20 class.[2] We have described elsewhere[3] how we have compared the levels of this class of lipoproteins (and of other serum lipid fractions), estimated serially during life in approximately 800 patients permanently confined to our hospital, with the amount of atherosclerosis found in 50 of these patients who died and were examined at autopsy. Our procedure was quite different from that employed by Gofman[2] and by others in that we did not assume that a person without signs and symptoms had normal arteries; rather, we measured as accurately as possible the amount of sclerosis present at autopsy, and compared this evidence of sclerosis with the serum lipid picture present during life. Our impression from the study of the first 50 fatalities in the series was that "the Sf 12-20 and Sf 20-100 classes of lipoproteins showed no relationship to the degree of atherosclerosis. . . . Their diagnostic importance for occult human atherosclerosis must therefore be taken as unproved in this preliminary series."[3]

Since the above study was initiated, Gofman has changed his "diagnostic" procedure several times. Instead of relying upon the Sf 12-20 class of lipoproteins he developed first what he called the "atherogenic index".[4] He postulated that the Sf 12-400 lipoproteins deserved approximately 1.75 times the crediting per mg. % that the Sf 0-12 lipoproteins required. The coronary

*From the Clinical Investigation Unit of Westminster Hospital, Department of Veterans' Affairs, and the Collip Medical Research Laboratory, University of Western Ontario, London, Ont.

risk was said to rise with increasing atherogenic index values. The index (A.I.) was calculated as follows:

$$\text{A. I.} = \frac{\text{(Std. Sf 0-12 in mg. \%)} + 1.75\ \text{(Std. Sf 12-400 in mg. \%)}}{10}$$

The data obtained from the first 50 fatalities in our series allow us now to calculate the atherogenic index from the serum of each individual, and to compare the results with the degree of coronary atherosclerosis found at death and autopsy. The present report deals with this comparison first.

While we were engaged in these calculations Gofman again modified his procedure.[5] He reduced the relative importance of the Sf 12-400 class from 1.75 times to 1.6 times, referring to this new index as the "alpha value", and he elaborated a new method of evaluation—the "accumulated coronary disease value" (A.C.D. value) in which the factor of age is taken into account. The second part of the present report will deal with the comparison of these new values with the findings in our series of 50 fatalities.

MATERIAL AND METHOD*

The clinical material, the procedure for estimating the serum lipid fractions during life, and the method of evaluating the severity of atherosclerosis at autopsy have been described in our original paper.[3] To avoid ambiguity we are repeating them here, almost verbatim. The only differences are that (1) only the standard Sf serum lipoproteins will be discussed, and (2) our present comparisons are confined to the coronary arteries, since they are the only vessels about which Gofman has made any claims.

The serum lipoproteins are being determined serially on 800 male patients who are permanently confined to hospital. The first survey began in April 1953. A second survey was carried out six months later and thereafter surveys were and will be made annually. At each survey 50 c.c. of venous blood is withdrawn from each patient shortly after breakfast. After maximum clot retraction the blood is centrifuged and the serum drawn off. A 10 c.c. aliquot of each sample is placed in a serum bottle and shipped in wet ice by air mail, from London, Ontario, to Montreal, Quebec, for estimations of the standard Sf 0-12, 12-20, 20-100, and 100-400 classes of lipoproteins. These estimations are carried out soon after the arrival of the specimen at the Ultracentrifuge Laboratory which is maintained by the Department of Veterans' Affairs at the Department of Chemistry, McGill University. The findings in these examinations are retained in Montreal until all of the estimations of the severity of coronary atherosclerosis in any one patient are concluded at our hospital. At this time, average levels of the various lipoprotein classes are calculated in those cases in which more than one estimation has been made during life.

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When a patient dies and comes to autopsy, the degree of coronary atherosclerosis is evaluated using six different indices of the severity of the disease—morphological grading, measurement of the thickness of the largest plaque, determination of the total amount and the concentration of lipid and of calcium deposited.

Morphological grading is carried out on the entire epicardial portions of the coronary arteries, which are removed from the heart and stripped of their outer coats to remove contaminating fat. The severity of disease is evaluated by the criteria of Davis and Klainer[6] in which the degree of stenosis produced by the largest plaque is the critical feature. A severe grade (+++) means that the lumen, at one point, is so encroached upon that it is reduced to less than 50% of its usual diameter. A slight grade (+) means that no plaque encroaches perceptibly upon the lumen. A moderate grade (++) means that the stenosing quality of the largest plaque is intermediate in type.

A small segment of the largest plaque is then excised, fixed in formalin, embedded in paraffin, sectioned, and stained with hæmatoxylin and eosin. The maximal thickness of the intima from the lining endothelium to the internal elastic lamina is measured with a micrometer eye-piece, and an index called "plaque thickness" thus obtained.

The remainder of the specimen is then referred to the chemical laboratory where estimations of the indices of total lipid content, lipid concentration, total calcium content and calcium concentration are made. Important features of the method are that, on arrival in the laboratory, the fresh tissues are weighed at once and then subjected to alkaline storage as recommended by Haven, Bloor and Randall.[7] The total lipid content is estimated by the method of the same authors,[7] while calcium is estimated by the Clarke-Collip modification[8] of the Kramer-Tisdall method after the alkaline digest has been subjected to acid digestion.[9]

All of the above estimations are carried out independently by three distinct groups of workers. The ante-mortem serum lipoprotein estimations are done by one group, morphological grading and micrometry by another, and the tissue analyses by a third. There is no collusion between members of these three groups until all of the estimations have been completed. The atherogenic index, the alpha value, and the A.C.D. value are then calculated.

The comparisons between the ante-mortem lipoprotein indices and the post-mortem morphological and chemical findings are made by first segregating the post-mortem data for individuals into three natural groupings. Thus the series is divided into the three groups of morphological gradings—severe, moderate and slight. And again, the series is divided into the three groups of lipid concentrations—highest, intermediate and lowest. A similar division is made for the other four indices. This division into groups is based on the natural range of levels for the number of cases available and is made without knowledge of the ante-mortem serum lipoprotein findings. The next step is to eliminate the intermediate (or moderate) group and then to compare statistically the mean ante-mortem serum lipoprotein values in the remaining two groups by the method of Fisher.[10] Elimination of the intermediate groups is justified since the data for post-mortem groups are arranged in order of increasing severity. P values of less than 0.05 are regarded as being significant; those equal to 0.05 are considered to be of borderline significance.

OBSERVATIONS

The age distribution, the clinical data, and the immediate causes of death for the 50 patients in the series have been given in our previous paper.[3] The evidence supporting the conclusion that neither aging nor terminal loss

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in weight from wasting disease might invalidate the results of our statistical analyses is given in the same paper.

The comparison of the mean atherogenic index with the severity of coronary atherosclerosis, measured in six different ways, is given in Table I. It is seen that no significant relationship exists between this serum index and any of the six indices of severity of disease: in each comparison the value for P is greater than 0.10. Furthermore, there is no trend towards increasing atherogenic index values with increasing severity of disease.

TABLE I.

ATHEROGENIC INDEX (GOFMAN) WITH DIFFERENT GRADES OF CORONARY ATHEROSCLEROSIS

Index of sclerosis	*Atherogenic index with different grades of sclerosis* *Slight sclerosis*	*Moderate sclerosis*	*Severe sclerosis*
Morphological grade	50 ± 6* (8)**	55 ± 3 (20)	55 ± 3 (22)
Plaque thickness	59 ± 4 (11)	52 ± 3 (27)	56 ± 4 (12)
Total lipid	58 ± 4 (18)	52 ± 2 (19)	51 ± 5 (13)
Lipid concentration	57 ± 3 (17)	53 ± 3 (21)	52 ± 5 (12)
Total calcium	57 ± 5 (16)	51 ± 2 (19)	55 ± 4 (15)
Calcium concentration	56 ± 4 (19)	53 ± 4 (16)	54 ± 4 (15)

Severe cf. Slight: all P values > 0.10.
*mean ± S.E.M.
**number of cases.

In view of Gofman's comparison of the atherogenic index with the presence or absence of overt coronary artery disease in the living patient, we also compared the atherogenic index with the presence or absence of pathological evidence of the disease in the fatalities in our series. The results of this comparison are given in Table II, and again it is evident that no significant difference in atherogenic index values exists between the two groups.

Similarly, no significant relationships were encountered when the mean alpha values were compared with the severity of coronary sclerosis as measured in six different ways. Since the results of these comparisons were very similar to those obtained when the atherogenic index was used (Table I), they are not presented here.* And again, no significant difference in alpha value existed between groups with and without pathological evidence of disease (as in Table II).

TABLE II.

ATHEROGENIC INDEX (GOFMAN) IN CASES WITH AND WITHOUT PATHOLOGICAL EVIDENCE OF CORONARY ARTERY DISEASE*

	Number of cases	*Atherogenic index*	
Cases with lesions	20	56 ± 3	P > 0.10
Cases without lesions	30	53 ± 3	

*Pathological evidence of coronary artery disease was taken to be:
(1) The presence of a coronary thrombus or other occluding lesion;
(2) A myocardial infarct, old or recent;
(3) Sudden and unexpected death in cases with severe coronary sclerosis without an occluding lesion or an infarct.

We have had more difficulty in evaluating the importance of Gofman's "accumulated coronary disease value", an index in which both the alpha value and the age of the individual are taken into account. Unfortunately, Gofman's published tables and graphs of A.C.D. values give no data for individuals older than 70 years; since many of our patients fall in this older age group, we have been unable to use his procedure and have adopted a different method of evaluation.

If Gofman's concept of the relationship of lipoproteins, and hence alpha values, to the *accumulation* of coronary artery disease over a period of time is correct, then, by examining individuals who are of the same age group it should follow that persons with high degrees of coronary artery disease should have proportionately higher alpha values than those with low indices of disease. We have not found this to be so.

Alpha values for all individuals in the same age group have been compared with the severity of coronary atherosclerosis, measured in six different ways. The results are given in Table III; and here, for the convenience of the reader, the cases in each decade have been arranged in order of decreasing magnitude of alpha value. On casual examination of this table it is evident that no relationship exists between the alpha values and the severity of disease in individuals of approximately the same age group. Striking deviations from the Gofman theory are in fact apparent: for example, the case in the eighth decade with the highest alpha value (A-58-54) has a very slight grade of disease, while the case with the lowest alpha value (A-123-54) has a very high grade.

Finally, the data given in the last column of Table III show that pathological sequelæ of coronary atherosclerosis are no more common in patients with high alpha values than in those with low alpha values when the comparisons are confined to patients in the same age group.

*In every case the mean alpha value was slightly lower than the mean atherogenic index due to the difference in calculation factor.

TABLE III.

ALPHA VALUES VERSUS THE SEVERITY OF CORONARY ATHEROSCLEROSIS BY DECADES

Autopsy number	*Age*	*Average alpha value*	*Morph. grade*	* *Plaque thickness*	† *Total lipid*	‡ *Lipid Conc.*	** *Total calcium*	†† *Calcium Conc.*	‡‡ *Complicating lesions*
A 5 - 55	43	65.9	++	+	+	+	+	+	no
A 18 - 54	40	47.8	+++	+++	++	+++	+	+	yes
A 124 - 54	57	74.8	+++	+++	+++	+++	+++	++	yes
A 86 - 54	54	64.1	+++	+	+	+	++	++	yes
A 7 - 54	54	58.3	+	+	+	++	+	+	no
A 116 - 54	59	53.2	++	+	+	++	+	+	no
A 40 - 54	59	52.9	+	+	++	++	+	+	no
A 55 - 54	57	45.4	+++	++	++	++	++	++	yes
A 81 - 54	57	43.7	++	+	+	+	+	+	no
A 55 - 53	55	32.7	+	+	++	++	++	++	yes
A 19 - 54	60	76.4	+	+	+	+	+	++	no
A 79 - 54	68	72.5	++	+++	++	++	+++	+++	no
A 98 - 54	67	67.9	+++	+++	+++	+++	+++	+++	no
A 107 - 54	60	61.9	++	++	+++	++	+++	+++	no
A 17 - 54	64	58.2	++	++	++	+	++	+	no
A 75 - 53	64	52.9	++	++	++	+	++	+	no
A 71 - 54	69	52.3	+++	++	+	+	+++	+++	yes
A 73 - 54	65	52.1	++	++	++	+	+	+	no
A 103 - 54	64	51.8	+++	++	++	++	+++	+++	no
A 60 - 54	62	49.3	+++	++	+	+	++	+++	yes
A 83 - 54	62	46.3	++	++	++	++	++	++	no
A 89 - 54	64	45.4	+++	+++	+	+	++	+++	yes
A 91 - 54	68	44.0	++	++	++	++	++	++	no
A 14 - 54	60	39.0	+++	+++	+++	+++	++	+	yes
A 58 - 54	76	75.4	++	+	+	+	+	+	no
A 79 - 53	79	59.3	+++	++	+	+	++	++	yes
A 15 - 54	73	56.8	++	++	+	+	+	+	no
A 68 - 53	75	54.2	+	+	+	+	+	+	no
A 111 - 53	74	52.8	+	++	++	++	+	+	no
A 91 - 53	70	51.1	+++	++	++	++	++	+++	no
A 31 - 54	74	47.8	+++	++	+++	+++	++	++	no
A 38 - 54	70	43.5	+++	+++	+++	+++	+++	++	yes
A 9 - 55	77	42.6	++	+	++	++	++	++	no
A 63 - 53	73	38.9	+	++	+	++	+	+	yes
A 3 - 55	79	35.0	++	++	+++	+++	++	++	no
A 122 - 54	71	33.7	++	++	++	++	++	+	no
A 123 - 54	71	26.1	+++	++	+++	+++	+++	+++	no
A 2 - 55	88	94.9	+++	++	+	++	+	+	yes
A 112 - 54	84	71.6	++	++	+++	++	+++	+++	yes
A 82 - 54	82	57.3	+++	+++	++	+++	+++	+++	yes
A 70 - 53	84	54.9	+++	+++	+++	+++	+++	+++	yes
A 76 - 54	85	48.9	++	+++	+	++	++	+++	no
A 93 - 54	82	45.8	++	++	+	+	++	++	no
A 114 - 54	83	44.7	+++	+++	+++	++	+++	++	yes
A 117 - 54	88	41.8	+++	++	++	++	+++	++	yes
A 8 - 54	85	39.1	+++	++	++	++	+++	+++	yes
A 82 - 53	81	33.5	++	+++	+++	++	+	+	yes
A 106 - 54	80	29.6	++	++	+++	+++	+++	+++	no
A 72 - 54	83	22.0	+	++	+	+	+	+	no
A 116 - 53	92	67.6	+++	++	++	+++	++	++	yes

*Plaque thickness in microns: + = < 1000; ++ = 1000 - 2000; +++ = > 2000.
†Total lipid in mg.: + = < 50.0; ++ = 50.0 - 99.9; +++ = 100.0 and up.
‡Lipid concentration in mg.%: + = <4.0; ++ = 4.0 - 5.9; +++ = 6.0 and up.
**Total calcium in mg.: + = < 10.0; ++ = 10.0 - 49.9; +++ = 50.0 and up.
††Calcium concentration in mg.%: + = < 1.0; ++ = 1.0 - 2.9; +++ = 3.0 and up.
‡‡Complicating lesions denotes presence or absence of pathological sequelæ of coronary atherosclerosis: a coronary thrombus or other occluding lesion, a cardiac infarct, or sudden death in association with severe coronary sclerosis but without an acute occlusion or infarct (acute coronary insufficiency).

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DISCUSSION

The results presented in this paper speak for themselves. One cannot escape the conclusion that the diagnostic value of the atherogenic index, the alpha value, and the accumulated coronary disease value for occult coronary sclerosis in the living patient is still unproved. Whether or not this conclusion will have to be modified when our series is enlarged remains to be seen, but at the moment there would appear to be no justification for using any of Gofman's indices as clinical tools.

Certain changes may have to be made in our assessment when the studies are extended: in particular, cognizance may have to be taken of the possibility that derangements in lipid metabolism are episodic, not permanent. It has been claimed that atherosclerosis is a disease which may take years to develop and which may persist for some time after the causative agent has ceased to act.[11] And in this regard, our present evaluations are based on serial determinations of the serum lipoproteins over a period of only 30 months, far short of the time needed to reveal a metabolic derangement of an episodic type. However, it should be borne in mind that Gofman has never insisted on more than one lipoprotein estimation from an individual for his forecast of incipient coronary artery disease.

In any event, we intend to persevere for an indefinite period in our documentation of the serum lipid levels in living patients, and of the severity of atherosclerosis in fatalities. When new claims about the etiology of the disease are made we will have an opportunity of assessing their validity.

SUMMARY

Gofman's "atherogenic index", "alpha value", and (by inference) his "accumulated coronary disease value" have been determined serially during life in a large series of patients who are permanently confined to hospital, and the findings compared with the severity of coronary atherosclerosis found at autopsy. The results in the first 50 fatalities in the series are reported. No relationship has been found to exist between these indices or values and the severity of the disease.

We wish to acknowledge the assistance of Professor R. J. Rossiter, D.V.A. consultant in biochemistry, and of Dr. J. B. Derrick who have given valuable advice and criticism throughout the entire course of this investigation. We are also indebted to Professor Carl Winkler and Dr. R. F. Robertson and their staff of the D.V.A. Ultracentrifuge Laboratory, McGill University, for the lipoprotein estimations; to Dr. G. P. Henderson of the Department of Mathematics, University of Western Ontario, for advice on the interpretation of Gofman's indices; and to various members of Westminster Hospital staff: Miss Dorothy Marsh, Mr. T. Moffatt, Mrs. Grace Strickland, Mr. Don Pulham, and Mr. Sam Elder.

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RÉSUMÉ

Les auteurs ont entrepris de vérifier les assertions de Gofman au sujet de sa méthode de prédire le degré d'athérome des artéres coronaires, basée sur le taux des lipoprotéines du sérum. Les termes "index athérogène" ainsi que "valeur de maladie coronarienne accumulée (valeur alpha)" sont définis. Les lipoprotéines sont groupées en quatre classes (Sf 0-12, 12-20, 20-100, 100-400) d'après leur séparation à l'ultracentrifuge. Les spécimens anatomopathologiques sont évaluées par rapport à la sévérité de la maladie d'après la morphologie, l'épaisseur des plus grosses plaques, la quantité globale et la concentration des lipides ainsi que les dépots de calcium.

Dans une série de 50 cas minutieusement suivis par les auteurs, aucune corrélation n'existe entre l'index athérogène et les six critères employés dans la classification des spécimens pathologiques. La valeur alpha ne supporte pas mieux la comparaison. En dépit de ces résultats décevants, les auteurs ont décidé de continuer leurs recherches dans ce sens puisque les désordres du métabolisme des lipides sont épisodiques et que l'athérome peut continuer à évoluer même après que l'agent en cause ait cessé d'agir. M.R.D.

R.C.A.F. CEMETERY, KIEL, 1956

Maybe, dear son, some yesteryear you stood
Beside this tree, on an Algoma hill,
Gazing entranced upon Superior's flood,
Your young heart throbbing to the magic's thrill.
Today I strew these ashes of its wood
Upon your lonely grave. In death's sleep, still
May they in mixing with this alien sand
Bring you the sunshine of your native land.

J. E. GIMBY

CARCINOMA OF THE INFRAPAPILLARY PART OF THE DUODENUM*

H. PROSEN, M.D. and
R. HASTINGS-JAMES, M.D.,
St. Boniface, Man.

ALTHOUGH cancer of the duodenum is said to form about 0.3% of all intestinal carcinomata, reports of diagnosis before operation or post mortem are rare. It might be expected that cancer would be the most common in the first portion of the duodenum, in view of the well-known tendency to ulceration in this region, but it is found that, if growths arising in the neighbourhood of the papilla of Vater be excluded, the incidence is approximately equal in all three portions.[1, 2]

This presentation of a case of carcinoma occurring in the infrapapillary portion of the duodenum is thought to be of interest since, up to 1953, Poer[3] was able to find in the records only 17 such cases successfully resected and of these only approximately one-third had been correctly diagnosed radiologically before operation.[4]

CASE REPORT

Mrs. X., age 55, was admitted in May 1952, complaining of occasional weakness, dizziness and epigastric pain of some 30 years' duration, becoming worse recently. She had noticed some dark blood in her stools. The only relevant positive finding on investigation was that her hæmoglobin value was 41%; this was raised to 72% after transfusion. She was discharged in June without a diagnosis being established. At that time she also complained of menorrhagia, which gave rise to some doubt as to the cause of the anæmia. She was treated by x-ray therapy and an artificial menopause induced.

She was seen again in July 1953, complaining of tiredness, weakness and malaise, and was readmitted to hospital when her hæmoglobin value was found to be 44%. Her stools contained occult blood. No cause for the bleeding was discovered, despite extensive x-ray investigation. However, on one occasion the possibility of a duodenal ulcer was raised. She was treated medically for her anæmia and was discharged, still feeling weak and becoming tired easily.

Her latest admission was in January 1955, with complaints of palpitation and sweating. Her weight was 156 lb., a loss of 40 lb. as compared with her weight on her first admission. Her blood pressure was 185/95 mm. Hg; the hæmoglobin value was 69%. No other positive findings were disclosed. During her stay on this occasion, her stools continued to be positive for occult blood and her hæmoglobin value slowly fell to 50%. Bone marrow puncture, gastric analysis and gastroscopy were all negative. Two or three attempts were made to demonstrate a lesion in the œsophagus, stomach and first part of the duodenum, but without success. The question of a small bowel abnormality as a source of bleeding was raised, and on one or two of the films it was felt that there might be some abnormality in the region of the duodeno-jejunal junction. Accordingly, a further examination was performed to investigate these points, using Baridol, and this was successful in showing clearly a constricted area in the terminal portion of the duodenum, with destruction of the mucosa and a concentric filling defect. The appearances were thought to be classical for a carcinoma (Fig. 1).



Fig. 1.—Spot film of duodeno-jejunal junction showing site of carcinoma.

Laparotomy was performed by Dr. J. McGoey and Dr. R. Lee on February 18 and a tumour was found in the fourth part of the duodenum. There were no visible signs of metastases, and part of the duodenum and the first loop of jejunum were resected.

Pathological Report.—The gross specimen consisted of a portion of duodenum measuring 17 x 5 cm., the serosa being smooth and shiny; the mucosal pattern was normal except at one end, where there was a firm cauliflower-like necrotic lesion extending to the end of the specimen and measuring 6.5 cm. in length (Fig. 2).



Fig. 2.—Gross specimen, showing junction of normal mucosa and polypoid infiltrating growth.

The cut section showed the entire wall to be involved in tumour growth; there was a papillary lesion composed of columnar tumour cells arranged in glandular formation and infiltrating the submucosa and the muscularis. In some areas tumour cells extended out to the subserosal fibrous tissue and fat (Fig. 3). Pathological diagnosis: infiltrating adenocarcinoma, grade II, Duke's "C".

*From the Departments of Gastroenterology and Radiology, St. Boniface Hospital.

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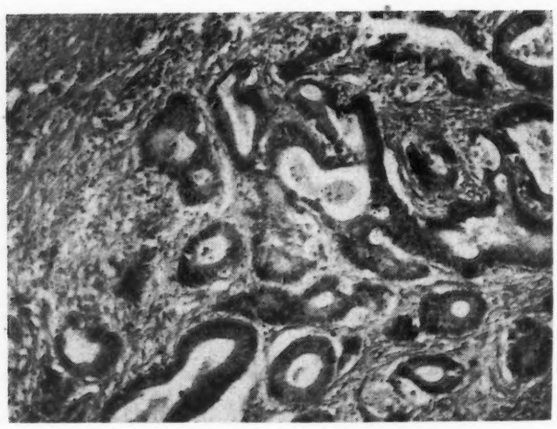


Fig. 3.—Microscopic appearances, showng infiltrating adenocarcinoma.

DISCUSSION

In most of the cases reported, the patient has suffered predominantly from effects of obstruction which may be partial, complete or intermittent. Abdominal pain and flatulence with weight loss and cachexia are among the leading symptoms. There is also a tendency to hæmorrhage and occasionally, as in the present case, unexplained anæmia may be the presenting symptom.

The difficulty of finding these hidden cancers may be very great, the region near the duodenojejunal flexure being a favourite site where they tend to lie behind the barium-filled stomach. It is likely only to be possible to see such a lesion and to get satisfactory films of it if deliberate search of this region is made, and it may be necessary to employ manœuvres such as tilting the patient head-down, in order to clear the area of superimposed shadows. Thus it is that the lesion is usually already far advanced by the time diagnosis is made and when secondary effects, such as duodenal obstruction, have served to draw attention to the affected area. The present patient was probably suffering from effects of the lesion for some three years before it was finally discovered. Additional difficulty was encountered in that the patient at one time suffered from menorrhagia, and on another occasion the possibility of a duodenal ulcer was raised, which tended to confuse the source of the unexplained anæmia.

Unfortunately the prognosis in these patients is poor and they tend to have metastases at an early stage. In the present patient the lesion was successfully resected and there was no apparent metastasis. She is alive and well a short time after the operation.

We should like to thank Dr. F. Burgoyne for contributing the pathological report.

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A REVIEW OF HERNIAL REPAIR, 1945 - 1951

(SHAUGHNESSY HOSPITAL)

HERVEY L. JACKES, M.B., *Vancouver*

IN THE PERIOD from February 1945 to December 1951, 1,000 operations for repair of all types of hernia were performed by the surgical staff of Shaughnessy Hospital. For this review of the results, we were able to contact 771 (77.1%) of the people on whom these operations were performed. I personally examined 565 of these people. The remaining 206 were examined by their local medical men, whose reports are on our files.

The elapsed time in the follow-up of 771 herniotomies was:

Years	*Number of cases*	*Percentage*
9	60	7.7
8	205	26.5
7	132	17.1
6	100	12.9
5	85	11.4
4	92	11.4
3	97	12.5

The minimal follow-up was three years; 76% of the series have been followed up for more than five years.

The age incidence in this series of 771 cases was:

Under 19	0.06%
20 - 29	15.1%
30 - 39	15.8%
40 - 49	13.4%
50 - 59	18.5%
60 - 69	29.0%
70 - 79	6.9%
80 and over	0.03%

It is interesting to note that the largest percentage age group was 60-69 years, and that 67.8% were over 40 years of age.

TYPES OF HERNIA

	Number	*Percentage*
Indirect inguinal	421	54.6
Direct inguinal	200	25.9
Direct and indirect inguinal	55	7.1
Femoral	32	4.1
Incisional	43	5.5
Umbilical	9	1.3
Epigastric	11	1.3

In addition, the following types of hernia were repaired.

	Number
Bilateral inguinal	124
Strangulated	6
Incarcerated	18
Femoral following inguinal repair	11
Associated femoral and inguinal	2
Sliding hernia	2

TYPE OF REPAIR

Halsted	347 (47.3%)	Gallie	5
Bassini	214 (29.2%)	Femoral approach	5
McVay	45 (6.1%)	Tantalum mesh	3
Fascial patch	27 (3.6%)	LaRoque	2
Simple apposition	25 (3.4%)	Wangensteen	1
		McArthur	1
Mayo	19 (2.6%)	Bloodgood	1
Henry	18 (2.6%)	Lotheisen	7
Ferguson	13 (1.7%)		

In some cases we were unable to identify the method of repair employed because of faulty records.

In 94 cases, in the inguinal repair group, a relaxing incision was used. In this group where this procedure was used, there was only one recurrence.

SUTURE MATERIAL

Steel	55.5%
Steel and linen	19.5%
Silk	12.8%
Chromic catgut	4.2%
Chromic catgut and steel	0.5%
Silk and steel	0.8%
Linen	6.2%

It is our policy to resort to early ambulation, with one day in bed in all uncomplicated cases. In cases in which a fascial patch repair is made, the number of days in bed is increased to five.

POSTOPERATIVE COMPLICATIONS (771 HERNIOTOMIES)

Ilio-inguinal causalgia	9
Spinal headache	16
Hæmatoma	7
Atrophy of testicle	8
Wound infection	38
Thrombophlebitis, superficial	1
Thrombophlebitis, deep	1
Chest complications: Pneumonitis, Atelectasis, Pneumonia, Bronchitis	14
Pulmonary embolus	1
Ileus	1
Hemiplegia	1
Incision into the bladder	2
Epididymitis	1

In all cases but one, the infection was minor and did not prolong the period of convalescence. Cultures were taken in each case.

INGUINAL HERNIA

The total number of inguinal herniæ in this series was 538; of these 370 were indirect, 124 direct, and 44 direct and indirect.

TYPES OF REPAIR

Halsted	47.0%	LaRoque	0.37%
Bassini	29.0%	Bloodgood	0.18%
McVay	6.0%	Tantalum	0.37%
Ferguson	1.7%	Undetermined	15.38%

In our series of 538 inguinal hernias operated on for the first time, the recurrence rate for the 370 indirect ones was 3.7% and for the 124 direct ones 12%. None of the 44 direct and indirect recurred.

An effort was made to determine the incidence of recurrence with respect to the type of original repair. It appeared to be 3 to 1, Bassini vs. Halsted. In 86.6% the recurrence appeared to be of the same type as was reported in the original repair; 13.4% had a different type of recurrence. It was further noted that in some of the repairs for recurrence the condition found was apparently an untouched indirect sac. It would appear that in the repair of an original direct hernia an indirect sac had been missed. The number of recurrences after a second repair was 5 out of 66, a recurrence rate of 7%.

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TABLE I.

ELAPSED TIME BEFORE RECURRENCE OF HERNIA

Age group in years																												
20 - 29...						1	3	1	4			1		1														
30 - 39...	1		2	1	1		7	5	6	2		2	1		1			1										
40 - 49...			1		2		4		3		1	2	2	1		2			1						1			
50 - 59...	4	2	1				11	4	2	4	1					1	1							2				
60 - 69...	2		2		2		3	4	7	1	1		2			1	1		1								1	1
70 - 79...				1			1	1	1				1					1								1		
80+.....																									1			
	1	2	3	4	6	8	1	2	3	4	5	6	7	8	9	10	11	12	13	15	18	20	24	25	27	28	29	30
Time in	Months						Years																					

The number of recurrent hernias repaired after a primary operation elsewhere was 82. In this group there were three recurrences (3.6%). Two cases had two previous repairs. One case had three previous repairs. The over-all recurrence rate of primary and recurrent repairs was 5.1%. There was one death.

FEMORAL HERNIA

Twenty-six cases had been primarily treated here, while four had been primarily treated elsewhere and appeared with a recurrence. The Henry approach was used in 18, the Lotheisen in seven and the femoral approach in five. There was one recurrence, after three years, and one immediate postoperative complication (hemiplegia). There was one death. In this series we had 11 cases of femoral hernia after an inguinal repair. The other three recurrent hernias had been repaired by a femoral approach.

VENTRAL HERNIA

There were eight cases of umbilical hernia, nine of epigastric hernia and 33 of incisional hernia. One epigastric hernia and five incisional hernias recurred (a recurrence rate of 12%). The recurrences in the five cases of incisional hernia are summarized below.

(1) Recurred in one year; postoperative bowel obstruction; infection; linen sutures. (2) After gastric resection, recurred in one year; no infection; silk sutures; re-repaired—fascial patch; wire sutures; good result. (3) After operation for gunshot wound; no infection; silk sutures; recurrence in three months; re-repaired—fascial patch; wire sutures; good result. (4) Gunshot wound, abdomen—ileus; recurrence in 10 days; re-repaired—fascial patch; wire sutures; good result. (5) After gastrectomy; recurrence in 10 days; evisceration; wire sutures.

CONCLUSIONS

It is not the purpose of this survey to discuss all aspects of the subject, but rather as a result of this study to make certain deductions from the material obtained.

1. Fully 60% of our cases have been in the so-called old-age group. We have found that age is no deterrent to the surgical repair of hernia in this group. The complications are the same in all the groups. The results compare favourably with those in other groups. Operation relieves the older man of the necessity of wearing a truss and prevents the catastrophe of a future strangulation.

2. Early ambulation is, we believe, an advance over the previous regimen of longer bed rest and, unless there is some complication, we insist on our patients getting up the next day. We feel that this minimizes the possibility of pulmonary and vascular complications. In cases where a fascial patch is employed, we arbitrarily keep the patient in bed five to seven days.

3. We believe that in the older age group, in addition to the usual preoperative check, a genitourinary investigation is indicated; if symptoms of urinary retention are present, the condi-

tion should be rectified before surgical repair of the hernia.

4. It is our practice in bilateral herniæ to perform two-stage operations. In this group we had 62 cases, making 124 operations. The elapsed time between the procedures was about three weeks. In this group we had a recurrence in three cases, a recurrence rate of 2.4%. It is interesting to compare this figure with the recurrence rate for the total number of first inguinal herniotomies, which was 3.7%. In no case have we resorted to bilateral repair at one procedure.

5. In this series we have had 11 cases of femoral hernia after inguinal repair. We believe that undue tension placed on Poupart's ligament in the ordinary repair of an inguinal hernia elevates the roof of the femoral canal, permitting easier egress of a hernia in that region. To lessen the possibility of this complication, we believe that a properly placed relaxing incision should be used in all cases where there is any tension on the suture line. We have used this procedure in 94 cases, with only one recurrence.

6. The choice of suture material is usually the prerogative of the individual operator. In this series, in 75% of the cases, steel or steel and linen were used—linen for the closure of the sac and reinforcement of the posterior wall, #32 steel for the remainder of the repair. It is believed that steel sutures answer all the requirements. There is definitely less reaction around the suture line.

7. Towards the latter part of this series, in the older group we resorted to orchidectomy in increasing numbers, and have now carried out this procedure in 31 cases. We feel that we thus obtain a much sounder repair, particularly in the aged in whom the tissues are poor and the normal tissue planes are ill-defined. In this small series of 31, we have had no recurrences.

8. The types of hernial repair are legion, and the choice of repair rests with the individual. We believe that no set procedure should be instituted until the anatomical defect has been observed at operation and the proper procedure adopted to suit each individual case.

We believe that for primary repair of an inguinal hernia a properly devised Halsted repair will suffice, taking into consideration the following points: (1) Careful dissection of the sac, with adequate closure. (2) Careful closure of the internal ring. (3) Careful closure of the posterior wall. (4) Obliteration of the lower angle at the pubic spine, the so-called "zone of failure" mentioned by Ogilvie. (5) Use of the relaxing incision to relieve tension in the apposition of Poupart's ligament to the conjoined tendon. (6) Complete hæmostasis. (7) Assurance that there is not an associated direct as well as an indirect sac present.

In the repair of recurrent hernia, the best procedure to adopt is strengthening of the posterior wall with implantation of a fascia lata patch. In repair of femoral hernia, we believe that the Henry extraperitoneal approach is probably the best procedure, except in the case of a large strangulated hernia.

In 1950 we reported a follow-up on some 500 hernial repairs with a recurrence rate of 4.6%. That series was a one-year to four-year follow-up. This series is a three-year to nine-year follow-up and includes many of the cases reported in the previous series.

Our recurrence rate in this present series is 5.1%. This would suggest that a longer period of time is necessary to give a correct picture of the recurrence rate.

The first of the two patients who died was 74 years old, and had a strangulated femoral hernia, with resection of gangrenous bowel; he died four hours after operation. The second, aged 89, died 10 hours after operation for a strangulated inguinal hernia. Autopsy findings were negative.

SHORT-TERM GROUP THERAPY OF PATIENTS WITH PARKINSON'S DISEASE

Experience with three groups of patients from the Parkinsonian Clinic of the Massachusetts General Hospital has convinced the investigators that group therapy is a practical and effective means of helping patients adjust themselves to chronic illness. Such group psychotherapy should be handled by a medically trained person, and active participation on the part of the group leader is necessary. Patients with Parkinson's disease tend to become depressed and to withdraw from society, and both these trends are greatly improved by group treatment. Because of the chronic nature of the disease, and because patients are apt to deteriorate physically, group psychotherapy in Parkinsonism should not be prolonged. The authors feel that similar short-term group therapy might be advantageous in many chronic illnesses.—M. E. Chafetz *et al.*: *New England J. Med.*, 253: 961, 1955.

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Case Reports

APLASTIC ANÆMIA FOLLOWING SULFONAMIDE THERAPY

JAMES CALDER, M.D.,
SAMUEL HANSON, M.D.,
LESLIE KOVACS, M.D. and
MATTHEW MATAS, M.D.,* *Edmonton, Alta.*

THE PURPOSE OF THIS PAPER is to present a case of the rare occurrence of aplastic anæmia following the use of a triple sulfonamide mixture. The usual fatal blood dyscrasias associated with sulfonamide therapy are agranulocytosis, hæmolytic anæmia and thrombocytopenic purpura.[1] We were able to collect only eight previously reported cases of aplastic anæmia related to sulfonamides in English-language journals.[2-5]

A 5½-month-old Metis baby boy was admitted to Charles Camsell Indian Hospital on October 11, 1954, because of hæmorrhages from the nose, mouth, rectum and sites of intramuscular injections. He was well until September 21, 1954, when he was treated in a northern nursing station for an upper respiratory infection. He was given 300,000 units of penicillin, 0.9 g. of aspirin and 1.8 g. of triple sulfonamide mixture (sulfadiazine, sulfamerazine, sulfamethazine aa) daily for seven days, after which he seemed to recover completely. Six days later the same treatment was instituted for rising fever and two doses of 50 mg. of aureomycin were also given. After a week he was transferred to this hospital because of external bleeding of multiple origin. He had received a total of 9,800,000 units of penicillin, 10.8 g. of aspirin and 21.6 g. of sulfonamides.

The baby, a well-developed infant weighing 5,650 g. (12 lb. 8 oz.), was acutely ill. His temperature was 106° F.; his pulse was thready and could not be counted. The respiratory rate was 60 per minute. There was bleeding from the nose, mouth and rectum, and petechial hæmorrhages were present on the upper limbs. The spleen and liver were not palpable. There was no sign of upper respiratory or pulmonary infection and the chest radiograph was negative. The urine had a pH of 6.0 and contained an occasional trace of albumin and no sugar; on microscopic examination no red cells, pus cells or sulfonamide crystals were seen. The hæmatological findings in the peripheral blood are given in Table I.

The treatment consisted of repeated transfusions (Table I), 50,000 units of penicillin every three hours, 15 units of ACTH and 100 mg. of aureomycin daily. The fever rapidly subsided. The oral, nasal and rectal bleeding persisted. He bled occasionally from the site of injections and developed subcutaneous hæmatomas in the same areas. On the fourth day in hospital he had an increasing nuchal rigidity. The spinal fluid contained fresh blood but was otherwise normal. Bone marrow from the tibia on the fifth day in hospital showed a nucleated cell count of 8,260 per c.mm., with 55% lymphocytes, 8% myeloblasts, 27% myelocytes, 4% mature neutrophils, 3% normoblasts, 1% megakaryocytes and 2% reticulum cells. Three days before death, coarse moist rales appeared in both chest fields accompanied by high fever. The patient died on the eighth day of hospitalization after a sudden massive hæmorrhage from the nose and mouth. The urinary excretion was always satisfactory.

Necropsy Findings.—Numerous petechial hæmorrhages were present in the skin, gastrointestinal tract, lungs, pericardium, urinary bladder and leptomeninges. The lungs were also the site of extensive bronchopneumonia. The bone marrow of the long and flat bones was scanty and pale pink.

Microscopic examination of the bone marrow revealed a markedly hypocellular marrow. There was a marked diminution of erythropoiesis and platelet production. No megakaryocytes were found. There was diminution of granulocytopoiesis, and no forms beyond the myelocyte stage were observed in the smears.

Staphylococcus aureus (hæmolytic) was grown from the post-mortem culture of the heart blood.

TABLE I.

Dates	*Oct. 11*	*Oct. 12*	*Oct. 13*	*Oct. 14*	*Oct. 15*	*Oct. 16*	*Oct.18*
Hæmoglobin (g.%)	5.5	10.0	13.1	11.4	11.0		10.6
Erythrocyte count (millions)	2.8						
Reticulocytes (%)			0.4				
Leukocytes, total (per c.mm.)	560	970	920	820	1,280	560	410
Juvenile neutrophils %	0		2	1	0		
Band neutrophils %	10		0	1	2		
Segmented neutrophils %	4		6	8	3		
Lymphocytes %	82		87	85	88		
Monocytes %	3		5	5	7		
Eosinophils %	1		0	0	0		
Platelets (per c.mm.)		17,000					
Blood transfusion in ml.	150	300	150	150	125		150

COMMENT

Aplastic anæmia after long-term, excessive dosage of sulfonamide therapy in a male infant was observed. The anæmia was easily corrected by blood transfusions, though the bleeding tendency was not modified. The absolute number of polymorphonuclear cells in the peripheral blood was only temporarily and insignificantly increased by ACTH. There was a striking arrest of granulocytopoiesis in the bone marrow at the myelocytic stage. The infant died of staphylococcal bronchopneumonia and septicæmia in spite of continuous antibiotic therapy. All the eight previously published cases had a fatal outcome with terminal bronchopneumonia.

SUMMARY

A fatal case of aplastic anæmia in a 5½-month-old infant, weighing 5,650 g., who received 21.6 g. of sulfonamide mixture over a period of 15 days is reported.

*From the Charles Camsell Indian Hospital, Edmonton, Alberta.

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POTTER'S FACIES ASSOCIATED WITH POLYCYSTIC KIDNEY, WITH LAURENCE-BIEDL-MOON SYNDROME IN SIBLINGS

AGNES E. BIMBI-KOVACS, M.D.* and
A. F. HARDYMENT, M.D.,† *Vancouver, B.C.*

IN 1946, EDITH L. POTTER[1] published an article on the facial characteristics of infants with bilateral renal agenesis. On the basis of a series of 20 cases observed, this is what she said:

"Bilateral renal agenesis is associated with a type of facies so characteristic that the absence of kidneys can be diagnosed in most instances on this finding alone. The principal change consists of a mild increase between the eyes, a very prominent fold of skin arising at the inner canthus, a flattening of the nose, mild retraction of the lower jaw, and large, low-lying ears with incomplete cartilaginous development. Infants with extreme renal hypoplasia or massive polycystic changes in the kidneys, all of whom die because of renal insufficiency, may have somewhat similar facies and may have some resemblance to infants with complete renal agenesis, but the appearance is never as typical, and the presence of a kidney anomaly cannot be foretold with certainty."

We have encountered a case in which this typical facial appearance was associated with polycystic kidneys.

The rarity of this particular entity, and the fact that we were led to discover four siblings with uncommon congenital malformations, make us feel that this family is worth reporting. Of the five other children born to this mother, two are alive and well, one died of renal insufficiency associated with horseshoe kidney, and two are alive and have the Laurence-Biedl-Moon syndrome. All except one had extra fingers and/or toes.



Fig. 1



Fig. 2

Figs. 1 and 2.—Baby boy W. Clinical photograph showing Potter's facies and polydactylism.

Baby W., male, was delivered on January 28, 1955, in the Vancouver General Hospital, about four weeks before the expected date. Clinically, there were no signs of immaturity. Birth weight was 5 lb. 10 oz. The mother was gravida 6, and Rh negative group A, but none of her five children had shown evidence of hæmolytic disease. The mother had been followed up in the Obstetrical Outpatient Department since December 1954 because of bleeding on two occasions. The possibility of placenta prævia was ruled out by radiography. She had had antibodies at a level of 1:4 in this pregnancy; the level had dropped to 1:2 just before delivery. Labour lasted 5 hours and 20 minutes; although the presentation was breech, delivery was considered easy. The placenta showed signs of early separation.

The baby did not require resuscitation, although because of poor general condition he gave the attend-

*Assistant Resident, Health Centre for Children, Vancouver. (Head of the Department, Professor J. F. McCreary, M.D.)
†Clinical Assistant Professor, in charge of the New Born Nursery.

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ing physicians considerable concern; the cord was markedly jaundiced.

Examination revealed the following positive findings: High palate, flattening of the nose, recession of the chin, enlarged and low-set ears, increased space between the eyes, prominent epicanthic folds forming a wide semicircle on each side of the nose, flattening of the tip of the nose, prominent crease below the lower lip, six fingers on the right hand, big hands and feet, and generalized hypotonia (Fig. 1).

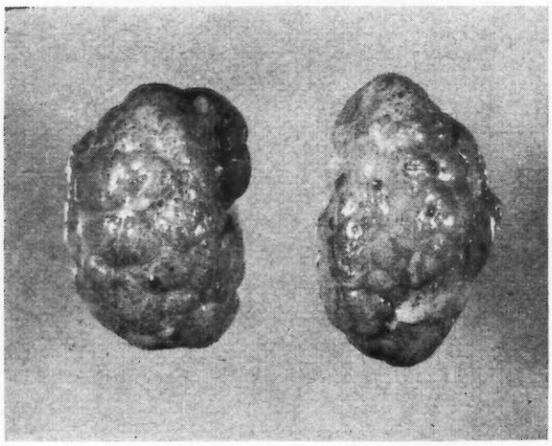


Fig. 3

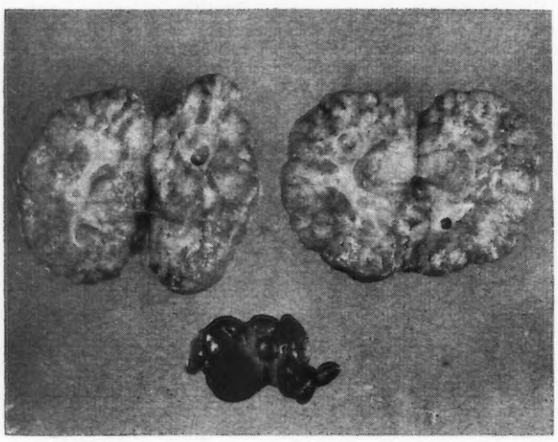


Fig. 4

Figs. 3 and 4.—Gross appearance of kidneys shows polycystic disease; there is also splenic lobulation.

Laboratory findings at birth were as follows: Coombs test positive; cord bilirubin 2.8 mg.%; hæmoglobin 12.2 g.%; red cell count 3,540,000; nucleated red cells 20%; reticulocytes 8.8%. Four hours after birth, the patient was treated with a replacement transfusion of 480 c.c. of Rh negative, group O blood.

Both parents were alive and well; the mother was 30, the father 31 years old. Repeated questioning failed to bring forth any major illness or malformations for three generations on either maternal or paternal side. Of the five siblings, the first was normal; the second child had six fingers on one hand and six toes on each foot. The third child had an extra finger. The fourth child had died at another hospital at one year of renal insufficiency; at autopsy, a horseshoe kidney had been found. The fifth child had an extra finger.

Laboratory data. For the first seven days, the patient had been excreting unknown amounts of very dilute urine, with specific gravity 1003—checked on several occasions—with protein varying from plus 3 to plus 2 and a negative microscopic analysis; later on, white cells and red cells were also seen.

A flat film of the abdomen taken on the third day of life showed no significant abnormality; barium meal revealed dilatation of both large and small bowel, obscuring both renal outlines. On the same date, films of the long bones were normal. On the seventh day of life an intravenous pyelogram failed to reveal any dye



Fig. 5

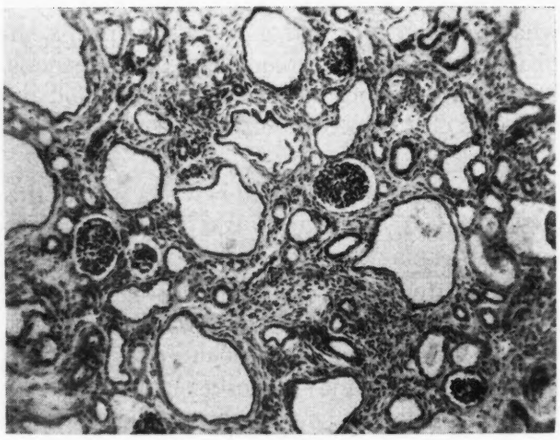


Fig. 6

Fig. 5.—H and E × 8. Fig. 6.—H and E × 120—Microscopic appearance of kidneys shows multiple cystic formations due to tubular dilatation.

within the urinary tract at any stage of the examination. The same result was obtained four days later. The non-protein nitrogen on repeated examination was 107 mg.%, 114 mg.%, and 120 mg.%; 12 hours before death, it rose to 180 mg.%. On the eleventh day of life, serum chloride level was 108 mEq./l., sodium 131 mEq./l., potassium 5.8 mEq./l., calcium 3.4 mEq./l., phosphate 7.6 mEq./l., CO_2 combining power only 1 mEq./l., and total proteins 5.6 g.%.

COURSE IN HOSPITAL

The baby was very listless throughout his life, weak, and unable to take adequate feeding by mouth. Fluids were administered by clysis and intravenously, not only to substitute for inadequate oral intake but also to combat the acidosis. Despite treatment, he gradually lost

weight and became quite emaciated. One day before death, he was very pale; respiration was noisy, laboured and rapid. He died on the 14th day of life. The clinical diagnosis was Potter's syndrome; polydactylism; hyperchloræmic acidosis; uræmia.

AUTOPSY FINDINGS

Only the positive findings will be described.

Gross examination. The body was that of an emaciated small baby, of about two weeks, weighing 1,875 g. On the little finger of the left hand, there was a projection issuing from the proximal phalanx, thought to be an accessory finger. No evidence of any nail formation was present on the small protrusion. Examination of the face showed low-slung ears, receding chin, and prominent naso-labial folds.

The right kidney weighed 23.5 g. and the left 22 g. (Figs. 3 and 4). The right kidney measured 3 x 5.2 x 1.8 cm., the left 3 x 5 x 1.5 cm. The outer surface of both kidneys showed fetal lobulation and was irregular, due to the presence of numerous small cysts measuring 1-3 mm. in diameter and containing clear fluid. Section revealed that the entire cortex and medulla were completely replaced by these small cysts. No renal tissue of normal architectural structure could be identified. The pelves and calices were not dilated and the ureters and bladder appeared normal. The spleen weighed 4.5 g. and was normal, except for its lobulated appearance. No other abnormal gross findings were encountered.

Microscopic examination. Both kidneys (Figs. 5 and 6) showed the microscopic structure of tubular polycystic disease. The cysts consisted of dilated tubules lined by flattened epithelium and imbedded in a cellular stroma in which scattered normal glomeruli were found. Complete nephrons could not be identified. In many areas the stroma was fibrous in character and rather abundant. The lungs showed œdema and atelectasis only. Other tissues were of normal histological structure.

SIBLINGS

Because of the fact that a previous child had died of renal insufficiency associated with horseshoe kidney and also because of the history of extra fingers and toes in the rest of the siblings, we examined each member of this family. The firstborn, a girl aged 9 at the time of our examination (February 1955), and the fifth child, a girl of 2, were normal, except for an extra finger on the right hand of the latter.

The mother complained that the third child, aged 5, was mentally slow, his speech retarded, his appetite "voracious", and he did not see well. He has been followed up for a period of one year at the Cardiac Outpatient Department because of a heart murmur.

He was a grossly overweight child, with obesity most marked on his thighs and legs. He had an extra finger and toe, his eyes were half closed as if he had photophobia, his speech was indistinct, his genitals small, his intellect dull. He had a loud, blowing systolic murmur over the entire precordium, maximal in the left fourth space and little affected by change of position. Blood pressure was 120/80 mm. Hg. In the cardiologist's opinion, he had a ventricular septal defect.

In another male sibling, aged 3½ years, findings were identical. He was very fat and obviously mentally retarded, and his speech was indistinct; he had an extra finger and toe, visual disturbance and small genitals.

In both of these cases, the provisional diagnosis of Laurence-Biedl-Moon syndrome was made. Fundoscopic examination showed pallor of the discs, attenuation of blood vessels, and retinitis pigmentosa without pigment, confirming the clinical diagnosis.

SUMMARY

1. A case of polycystic kidney with facial characteristics of renal agenesis is presented.

2. Laurence-Biedl-Moon syndrome, horseshoe kidney and polydactylism were present singly or in combination in four of five remaining siblings.

We should like to express our gratitude to Dr. J. F. McCreary, Professor of Pædiatrics, University of British Columbia, and Head of Department of the Health Centre for Children, Vancouver, for his advice and help in writing this paper.

We also feel indebted to Dr. W. B. Leach, Pathologist (Pathological Anatomy), Vancouver General Hospital, for his assistance in the preparation of the pathological report and photographs.

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RESULTS OF THORACOLUMBAR SYMPATHECTOMY FOR ESSENTIAL HYPERTENSION

In a three- to seven-year follow-up of 100 patients operated upon for essential hypertension, the mortality was 2%. Three-quarters of the patients had normal renal biopsies, confirming the impression that renal damage is a secondary manifestation. Headache was usually relieved. Most were relieved of visual disturbances, decompensation, vomiting and dyspnœa. As to general condition and ability to work, 85% of the patients were improved, 10% unimproved and 5% worse. The survival rates over five years were: 100% in group 1, 85% in group 2, 86% in group 3, 63% in group 4 and 45% in group 5. Thus surgery is indicated for group 4 and 5 patients as well as for those showing less severe signs.

The technique of the operation through a subcostal retropleural dissection of sympathetic chain from T6 to L3 is described.—H. A. Zintel *et al.*: *A.M.A. Arch. Surg.*, 71: 215, 1955.

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ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS IN A NORTH AMERICAN INDIAN GIRL*

LESLIE KOVACS, M.D., JAMES CALDER, M.D., MATTHEW MATAS, M.D., and SAMUEL HANSON, M.D., *Edmonton, Alta.*

A CASE of acute disseminated lupus erythmatosus in a North American Indian girl is reported. To our knowledge this is the first proved case reported in this race.

A 14-year-old Indian girl from Southeastern Alberta was admitted to a local hospital in September 1954. Three months before admission she complained of pain and swelling in both ankles, over which the skin was red and hot. During the ensuing three summer months she felt feeble, chilly, and feverish, and did not leave her room. Since her condition remained unchanged and the fever persisted, she was transferred after three weeks' hospitalization to the Charles Camsell Indian Hospital.

On admission the patient was well oriented and well nourished, but acutely ill, markedly orthopnœic even at rest and slightly cyanosed. The temperature was 104.4° F., pulse rate 154, respiratory rate 60 and the blood pressure 120/80 mm. Hg. No skin lesion was present on the face. The veins of the neck were distended. The heart was enlarged to percussion; the apex impulse could not be palpated and the heart sounds could not be heard over the apex. Scattered moist rales were heard over both lung fields and the breath sounds were decreased at the right base posteriorly, with dullness in that area. The liver was felt two fingerbreadths below the right costal margin in the midclavicular line and the edge was tender. The spleen was not palpable. Slight ankle œdema was present.

The summary of the laboratory findings on admission and on subsequent occasions is outlined in Table I (page 555).

The electrocardiographic tracing taken on admission showed a normal sinus rhythm, a PR interval of 0.20 second, a QRS interval of 0.04 second. The QRS complex was less than 0.5 mm. in all leads. The ST segments were slightly elevated in L_1, L_2 and aVF; T waves were low in all the leads. Subsequent tracings were similar to the first one except during digitalization, when the sinus rhythm was transformed to upper nodal or atrial rhythm. The x-ray picture of the chest on admission is shown in Fig. 1. Subsequent films had to be taken with portable x-ray apparatus in the antero-posterior position, which made comparison difficult.

Course and treatment.—The temperature and treatment are outlined in Fig. 2. We tentatively accepted the positive blood culture in the presence of the urinary findings as evidence of subacute bacterial endocarditis despite the absence of a cardiac murmur. The isolated streptococcus was highly sensitive to all the antibiotics, and antibiotic treatment was instituted (Fig. 3). The patient was placed on a salt-free diet, and when the fever subsided, the signs of cardiac failure were minimal. Pericardial aspiration yielded only 20 ml. of bloody fluid.

On the 31st hospital day she vomited some material resembling coffee-grounds, and passed black, tarry stools. A few hours later there were signs of cerebral anoxia and she lapsed into coma. There were no localizing neurological signs. The respiration was typical of air hunger. She was given 2,500 ml. of blood before she regained consciousness. She passed tarry stools for the following five days. More intensive antibiotic treatment

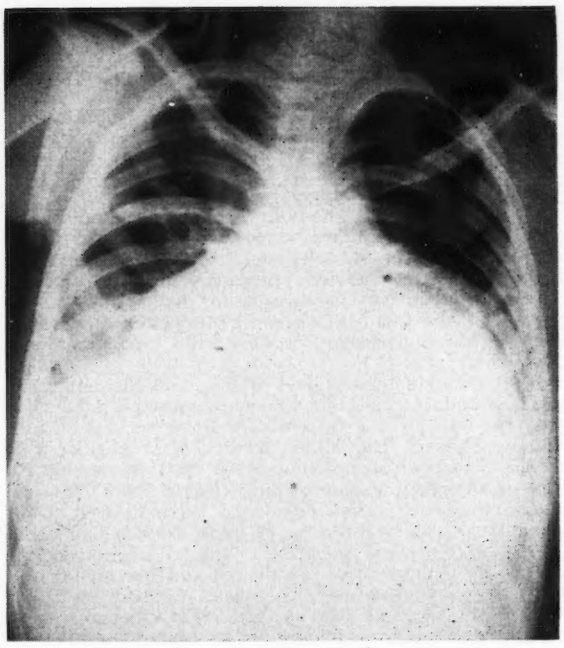


Fig. 1.—X-ray film on admission. There is a marked enlargement of the cardiac shadow and its appearance is compatible with the diagnosis of pericardial effusion. Some pleural effusion is present bilaterally. The hilar vessels are engorged and there is evidence of pulmonary congestion at both bases.

was instituted, but her temperature remained elevated. A second pericardial aspiration again yielded 20 ml. of bloody fluid.

On the 40th hospital day L.E. cells were demonstrated in the peripheral venous blood. This finding was confirmed on several occasions. Hormone therapy was started.

On the 54th hospital day signs of cardiac tamponade developed, and pericardial aspiration resulted in the withdrawal of 640 ml. of bloody fluid. Two days later another 100 ml. of bloody fluid was aspirated. The patient began to improve slowly. The cardiac symptoms were well controlled with digitalis.

On the 61st hospital day she developed recurring convulsions which started on the right side of the face, followed by generalized clonic contractions. The convulsive state continued unabated despite heavy barbiturate sedation given intravenously and orally. Ether had to be used to control the seizures. She lapsed into coma with spasticity of the right side, ptosis of the right upper eyelid and the mouth pulled over to the right. The right plantar reflex was extensor on one occasion, but on other occasions was equivocal. The pupils were dilated, symmetrical and non-reactive to light. The fundi were not remarkable. The blood pressure stayed normal and the pulse was regular. The spinal fluid showed normal dynamics and content. In the following 72 hours the chest progressively filled up with coarse, moist rales bilaterally. The temperature became markedly elevated, and terminally the blood pressure dropped to 80/40. Urine excretion became scanty during the final 24 hours. She died quietly on the 65th day of hospitalization.

At no time was any heart murmur present. The spleen was never palpable. The liver enlargement varied between one and two fingerbreadths below the costal margin. Ankle œdema was always minimal.

ANATOMICAL STUDIES

The positive findings at autopsy were as follows:

The right pleural cavity contained 300 ml. of cloudy yellow fluid. The left pleural cavity was completely

*From the Charles Camsell Indian Hospital, Edmonton, Alta.

obliterated by adhesions. The pericardial cavity contained 150 ml. of thin bloody fluid. Numerous fibrinous strands were present in the pericardial cavity, and a reddish fibrinous exudate covered the inner surface of the parietal pericardium and the surface of the heart. The heart weighed 350 g. and was larger than normal. The myocardium was a homogeneous dark brown and felt flabby. The lungs were of normal size and were moderately crepitant. Purulent exudate was present in the bronchial tree of each lung.

Filmy, fibrous peritoneal adhesions were present. The adrenal glands were larger than normal, each weighing 12 g. The kidneys were somewhat enlarged. The left kidney weighed 220 g. and the right 230 g. Their capsules stripped easily and their external surfaces were smooth. Medulla and cortex bulged on the cut surface and these were poorly differentiated. The spleen was of normal size and weighed 180 g. Its pulp was hæmorrhagic and quite soft. The brain weighed 1,300 g.

Microscopically, there was a severe inflammatory reaction in the epicardium. The inflammatory cells were polymorphonuclear leukocytes, lymphocytes and plasma cells. There was fibroblastic proliferation and new capillary formation. There was laying down of ground substances showing extensive fibrinoid change and metachromasia. The interfibrillar connective tissue in the heart muscle showed marked fibrinoid necrosis, as did the arterioles in the myocardium. Fibrinoid necrosis and metachromasia of the fibrous tissue of the valve cusps were seen. An extensive bronchopneumonia was present in the lungs. Small arteries and arterioles showed fibrinoid necrosis. There was marked chronic passive congestion in the liver. The central arterioles of the spleen had a typical periarterial concentric lamination of collagen. The adrenal cortex was hyperplastic and congested. In the kidneys wireloop lesions of glomeruli were present. The glomeruli were uniformly avascular and there was swelling and fibrinoid change in the capillary walls of glomerular tufts. Fibrinoid necrosis of cerebral arterioles was seen. Photomicrographs of the salient microscopic findings are presented in Fig. 3.

DISCUSSION

Disseminated lupus erythematosus was first described in 1845 by Hebra[5] and separated from the other forms of lupus as a clinical entity connected with the visceral manifestations by Kaposi in 1872.[8] Before the description of the L.E. phenomenon by Hargraves[4] in 1948 it was thought that the white race was more susceptible to the disease.[1] Even recently the statement was made that the acute form of disseminated lupus erythematosus was rarely encountered in coloured patients,[15] but several authors[3, 7, 11, 14] have found that the disease is quite common in pigmented races. The case presented is the first reported occurrence of acute disseminated lupus erythematosus in the North American Indian.

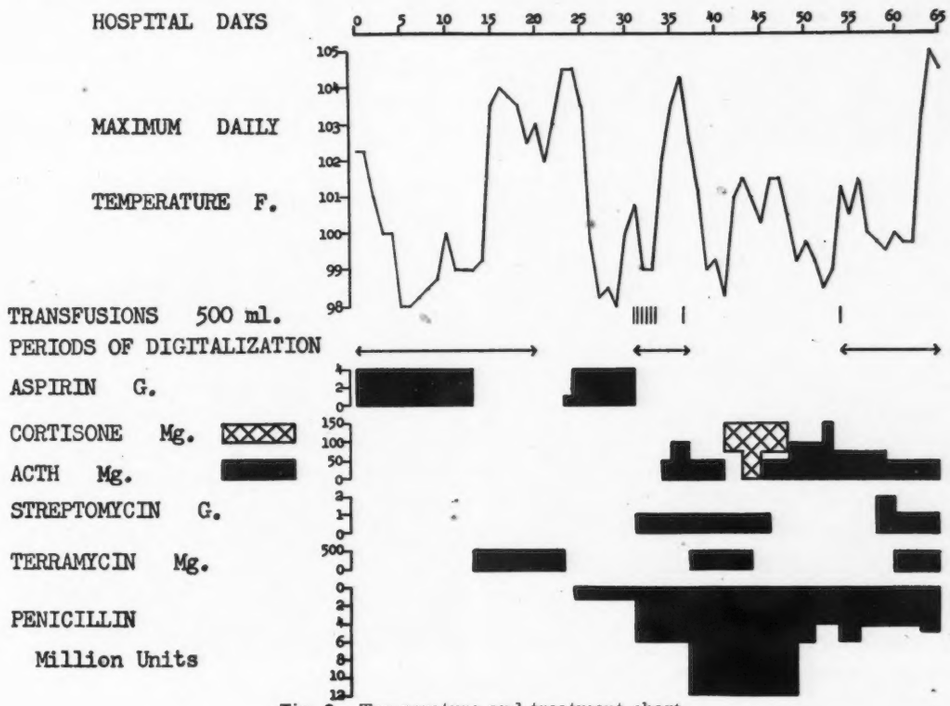


Fig. 2.—Temperature and treatment chart.

This patient had many of the characteristic findings of disseminated lupus. The laboratory and autopsy findings were typical. We encountered all the unfavourable symptoms mentioned by Tumulty, and 30 days of hormone therapy was of no value. Decubitus ulcers developed early in the disease and were very extensive. The pericardial effusion was massive, which is unusual for lupus,[2, 11, 14] and produced signs of cardiac tamponade. In 17 patients with cardiac tamponade reported by Williams and Soutter[16] lupus erythematosus was suspected as

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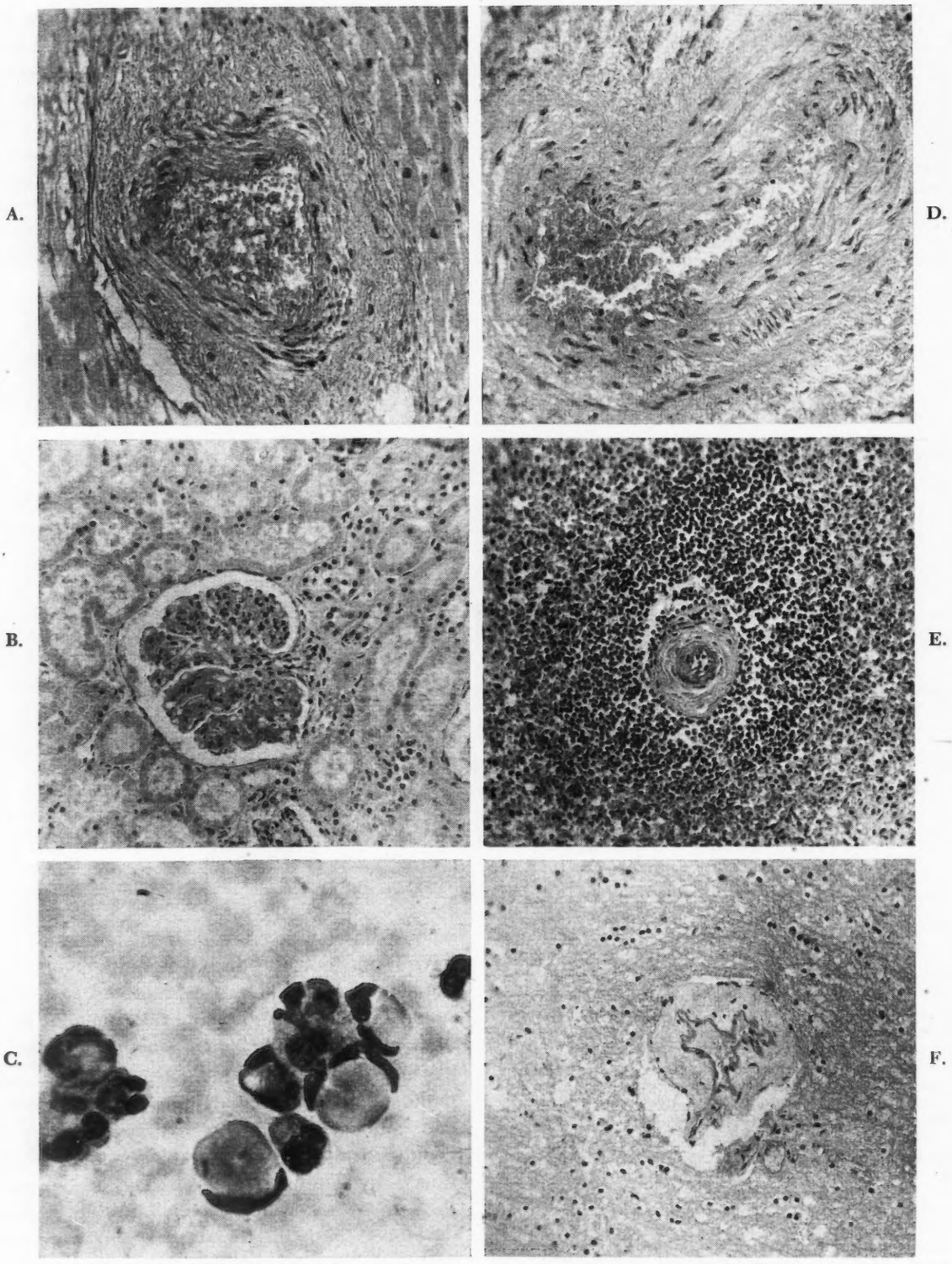


Fig. 3.—Photomicrographs. (A) Fibrinoid necrosis of arteriole in myocardium. H & E × 100. (B) Glomerulus showing the wire-loop lesion. H & E × 430. (C) Smear of the buffy coat of coagulated blood showing the L.E. cells. Wright. × 430. (D) Small artery in epicardium showing marked fibrinoid change. H & E × 430. (E) Arteriole in spleen showing typical onion-skin lesion. H & E × 100. (F) Cerebral arteriole showing fibrinoid necrosis and perivascular œdema. H & E × 100.

TABLE I.

SUMMARY OF LABORATORY DATA

Hospital days	*26*	*28*	*31*	*34*	*36*	*40*	*50*	*56*	*58*
Urine:									
pH	5.0			5.0	5.5	4.5	6.0	6.5	6.5
Albumin	neg.			3 plus	2 plus	neg.	trace	neg.	trace
Sugar	neg.			neg.	neg.	neg.	neg.	neg.	trace
WBC/h.p.f.	50-60			10-12	8-10	occ.	8-10	6-8	10-12
RBC/h.p.f.	occ.			numer-ous	50-60	occ.	30-55	15-20	——
Casts					hyaline granular	hyaline	hyaline granular		
Hb. g.%	7.03	6.80	2.50	9.40	7.00	9.10	9.10	7.90	
RBC millions/c.mm.	3.07	3.18			2.26	3.37	2.97		
WBC thousands/c.mm.	8.20	8.25		12.35	10.45	12.60	7.35	7.05	
PMN in %	86	90		90	79	44	88		
Platelets, thousands/c.mm.				76			134		
ESR mm./hour	131				124	105			
Serum proteins g.%	6.40						5.10		
A/G ratio	0.91						0.83		
BUN mg%	67.5			91.5	114.5	62.0	14.8	14.4	
Serum bilirubin mg.%			0.4			0.6	0.2		
Serum chlorides mEq./l.	103.6				88.0	93.5	101.8	81.5	93.3
Serum sodium mEq./l.	130.0				130.0	141.0		112.0	130.5
Serum potassium mEq./l.	6.0				2.6	3.2	3.4	3.8	2.4
L.E. phenomenon						present	present	present	present
Kahn, Kolmer, W.R.	doubtful						neg.		
Mantoux 1 mg. OT	neg.								
Antistreptolysin titre "O"						40 u.			
Blood cultures	S. viridans	sterile	sterile			sterile		sterile	
Pericardial fluid cultures			sterile			sterile		sterile	sterile

the causative agent in only one case. The upper gastrointestinal hæmorrhage was explained by us as the result of thrombocytopenia and congestion in the portal circulation. Prolonged aspirin therapy could have contributed to the bleeding tendency. On autopsy no ulcers or œsophageal varices were found to explain the massive bleeding. It was Osler[12] who first pointed out the frequency of gastrointestinal involvement in this disease; of his 11 cases three had bowel hæmorrhages and two gastric hæmorrhages. Seven of the 105 patients had abdominal pain, diarrhœa and hæmorrhage as a major complication in Tumulty's series; Dubois mentions a 10% incidence, though McGehee *et al.* collected only 5 cases of hæmorrhage out of 245 patients. Humphreys[6] considers gastrointestinal bleeding as a pre-terminal event.

Epileptiform seizures are frequently encountered in lupus, though macroscopic and microscopic findings in the brain may be lacking. They occur most frequently terminally. Terminal seizures occurred in 6 out of 20 cases reported by Klemperer *et al.*,[9] 3 out of 4 in the original description by Libman and Jacks[10] and 18 out of 105 in Tumulty's publication. Russel, Haserick and Zucker[13] mention a 15% incidence of epileptiform seizures in 144 cases, Jessar, Lamont-Havers, and Ragan a 9% incidence in 216 cases,[7] Dubois a 31% incidence in 62 cases. Russel *et al.* state that cortisone and ACTH are effective in controlling epileptiform seizures related to lupus.

The occurrence of bilateral extensive bronchopneumonia in spite of the heavy dosage of antibiotics illustrates the poor resistance of these patients to infection. Of the Johns Hopkins Hospital series[14] 42% died of infection.

SUMMARY

A case of acute disseminated lupus erythematosus in a North American Indian girl is presented. Administration of ACTH and cortisone was not effective. The patient's condition was complicated by massive gastrointestinal hæmorrhage, epileptiform convulsions, pericarditis and terminal bronchopneumonia.

Grateful acknowledgment is made to Dr. R. S. Fraser, University of Alberta Hospital, for his advice in the management of this patient.

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A CASE OF GASTRIC HÆMORRHAGE WITH UNUSUAL SEQUELÆ*

LIONEL MARKS, M.D., F.A.C.G., *Toronto*

THIS CASE is presented because of several unusual features and because the author had an opportunity to follow it up for a year after operation.

The patient, a man of 64, was admitted to the New Mount Sinai Hospital with a severe gastric hæmorrhage. On admission the patient was vomiting blood and passing black stools per rectum. The Hb value was 50% and red cell count 3,000,000. On admission he was given 500 c.c. of blood. The bleeding stopped and he became symptom-free. In less than one week his red cell count was up to 4,000,000 and his Hb to 67%.

He was said to have had a duodenal ulcer for the past 30 years and had had treatment off and on for the same length of time. There were five or six episodes of bleeding during this 30-year period.

When he improved on medical treatment in hospital and while discussion was going on whether the patient would agree to operation or not, another 500 c.c. of blood was given to him. A gastrointestinal series done at this time was inconclusive. The radiologist reported that the patient's stomach was filled with blood clots and no definite opinion could be given. While the patient was feeling well and on treatment for ulcer and the stools were free of occult blood, he sprang a severe hæmorrhage one morning at about 3.00 a.m. I found him unconscious in bed, his eyes rolled back, his skin moist and clammy, and his bed sheets covered with bright red blood. His pulse was 130, thready and weak; his blood pressure was 70/50 mm. Hg. An immediate transfusion of 1,000 c.c. of blood was given and on that day he was taken to the operating room. A laparotomy was done by Dr. Harold Grossman of the Surgical Staff. The operation was carried out with the intention of saving the patient's life rather than of curing him.

At operation, a small gastric ulcer with a great deal of induration was found in the mid-portion of the stomach along the lesser curvature. It looked benign and there was an open blood vessel in its centre. A thorough search was made for other bleeding points, particularly in the duodenum. The duodenum was found to be soft and pliable, with no evidence of disease. The ulcer and the induration were removed by a V-shaped incision. This was all that could be done at that time because of the patient's poor general condition. The stomach was sewn up and the patient returned to bed. He made an uneventful recovery.

*From the Department of Medicine, New Mount Sinai Hospital, Toronto.

The pathologist reported that the specimen was 3.4 x 3 x 0.6 cm. The acini were lined with columnar epithelial cells with nuclei of irregular size and shape and with heavily staining chromatin material. The acini penetrated into muscle coats of the stomach and extended to the periphery of the section. A diagnosis of adenocarcinoma of the stomach was made on this section by Dr. H. Pritzker of the Pathology Department of the New Mount Sinai Hospital.

Several attempts have been made to readmit this patient for further operation but he has refused. The patient was seen in my office and films were taken of the stomach after barium ingestion in October 1954, December 1954, and April 1955. These show no evidence of ulcer, growth or induration. There is no evidence of either gastric or duodenal ulcer and there is no evidence of any change in these films over the period of almost one year.

At examination in April 1955, approximately one year after operation, we find the radiographs as described above. The patient is in excellent health and has no gastrointestinal symptoms; he has gained weight; his appetite is good and his red cell count is 4,000,000. There is no evidence of any secondaries or of gastric carcinoma.

DISCUSSION

This case is presented as a case of severe gastric hæmorrhage, whose cause was diagnosed on section as gastric adenocarcinoma. The combination of a past history of bleeding from a duodenal ulcer and a present gastric carcinoma is very unusual. One wonders whether this patient has had a duodenal ulcer or whether he has had a gastric ulcer which has become malignant. I believe that the transfusion given to him in preparation for surgery saved his life. It is also extremely unusual to see no evidence of carcinoma of the stomach one year after local resection only.

GASTROINTESTINAL HÆMORRHAGE: THERAPEUTIC EVALUATION OF BIO-FLAVONOIDS

A group of workers from the New York Polyclinic Medical School report the results of treatment of 55 cases of gastrointestinal hæmorrhage with a bioflavonoid preparation (C.V.P. = flavonoids + ascorbic acid). The source of bleeding was very varied in this series, being from a peptic ulcer in 19 cases, from ulcerative colitis in 14 cases and from the rectum in 7 cases. Dosage was 300 to 600 mg. daily in capsule form by mouth. A high incidence of satisfactory results with prompt arrest of bleeding is claimed.—S. Weiss, J. Weiss and B. Weiss: *Am. J. Gastroenterol.*, 24: 523, 1955.

Special Article

MEDICAL RESEARCH IN TRAFFIC ACCIDENTS*

(A PLAN FOR STUDYING THE PROBLEM THROUGH RESEARCH UNITS IN CASUALTY WARDS OF TEACHING HOSPITALS)

HAROLD ELLIOTT, M.D., *Montreal*

IT IS BECOMING more and more apparent that the alarming increase of deaths and injuries from traffic accidents should be subjected to a nation-wide scientific survey along epidemiological lines. W. H. Welch in 1899 summarized the value of the epidemiological approach to disease when he said:

"It is evident that efforts to preserve health will be most intelligently and effectually applied when they are based upon an accurate and full knowledge of the agencies which cause disease."

Since World War II, the United States Armed Forces Epidemiological Board has made a co-ordinated effort, by assisted research, in many aspects of the problem. However, a full-scale study of the subject has never been carried out by the medical profession. The plan suggested below outlines one method of carrying out this survey in Canada.

THE FIELD OF TRAFFIC ACCIDENTS

Fig. 1 attempts to outline the factors and agencies at work in the traffic accident field. At Cornell Medical College, one of these factors, namely, auto crash injury, is being intensively studied with the co-operation of ten states. In this project the medical information about death and injury related to the automobile is gathered with the co-operation of the Departments of Health and the State Medical Society. The medical data are then correlated with other accident data obtained from the police. The Cornell auto crash injury research project illustrates the type of co-operative effort required. The plan suggested for Canada embodies the Cornell data-collecting method, modified so that the collection of data is carried out by research units in the teaching hospitals from coast to coast.

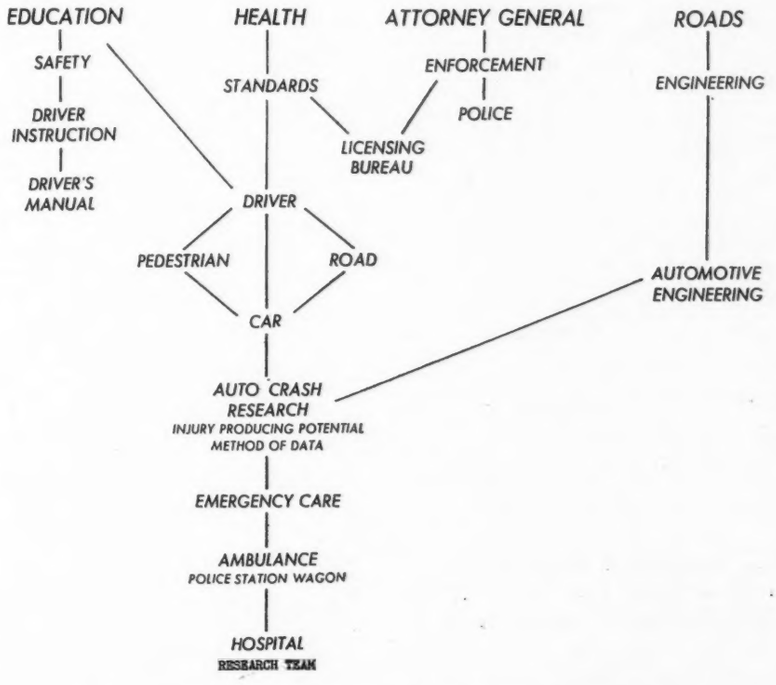


Fig. 1.—Faults in this traffic accident field are the cause of the rising accident rate. Yet for the past 50 years, safety has been the watchword, and the driver largely blamed. A new approach may be of help. It is our duty to search out these faults on a community-wide and nation-wide basis. After all, death and injury are the concern of the medical profession.

*From the Department of Neurology and Neurosurgery, Montreal General Hospital and the Queen Mary Veterans Hospital, Montreal. Presented to the Lafleur Reporting Society, February 21, 1956.

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CASUALTY WARD RESEARCH IN TEACHING HOSPITALS

Teaching hospitals are a focus for teaching, research and therapy. The place of the casualty ward research unit is shown at the key point in the traffic accident field (Fig. 1).

It is natural to have the research unit situated in these strategic locations.

The teaching hospitals are well equipped with specialized personnel, from public health to psychiatry, to assist a research unit in collecting these data. Since medical teaching is an important function of these hospitals, research data, obtained by a professional unit, can be readily passed on to the medical students. The death and injury rate, shown in Fig. 2, will be lowered when our medical graduates have the data and effectually apply it. If assisted grants are made available to research fellows, they will be able to study the traumatic episode in all its phases as part of their course in training for one of the fellowship degrees. Since the traffic accident field embodies all hospitals, these research fellows will have to enlist the co-operation of all the community hospitals in gathering the data.

CO-ORDINATING UNIT

Once the data are collected for each accident, they should be sent to a co-ordinating unit. This will enable many comparisons to be made on an epidemiological basis. The co-ordinating office should be staffed by a full-time medical research director, a statistician and three field men. The field men will check on the reliability of the sample data.

In order to carry this plan through to completion, a research foundation will be required.

CANADIAN MEDICAL TRAFFIC ACCIDENT RESEARCH FOUNDATION

Dean Lyman Duff suggested at the end of the Montreal Conference on Medical Aspects of Traffic Accidents, May 4-5, 1955, that a medical research foundation patterned on the Canadian Cancer Institute might render great service. It was also suggested that it should carry out an intensive study of the whole traffic accident field for a period of not less than five years. This Conference on the Medical Aspects of Traffic Accidents was international in scope and sought to gather all the available data in this field, as well as to outline a workable approach to the problem of traffic accidents in general.



Fig. 2

Many proposals are set out in the Proceedings of the Montreal Conference which will shortly be off the press. Through the kindness of the Sun Life Assurance Company of Canada, these Proceedings will be sent to university medical libraries. Other research studies in this field are suggested in this publication.

Endorsement from Other Official Bodies:

The Royal College of Physicians and Surgeons of Canada has endorsed the suggestion for the

setting up of an institute for medical research in traffic accidents. The Canadian Bar Association has appointed a representative to work with the nucleus committee. The Canadian Medical Association has appointed a central committee for traffic accidents with divisional representatives. Stimulating progress has been recorded in the work of these divisions. In addition, a combined conference between medicine and industry has been projected and endorsed by the Canadian Medical Association to consider the creation of such a separate foundation. Public-spirited men in the automobile industry have been approached and they have offered assistance. The proposed foundation is suggested in Fig. 3.

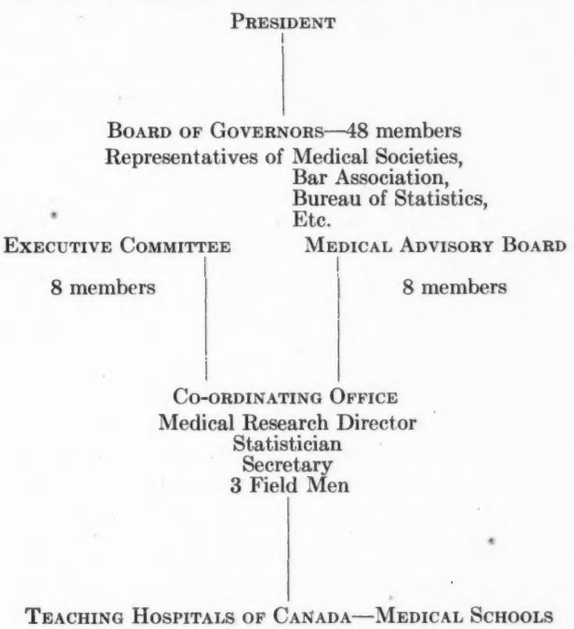


Fig. 3

CONCLUSION

The epidemiological approach to traffic accidents is outlined in a scheme for studying the traumatic episode in communities throughout the country. In order to carry out the study, funds from industry should be forthcoming. If this step materializes, the medical profession may be in a position to offer guidance and leadership in a new crusade.

MEASUREMENT OF BLOOD- AND FLUID-LOSS AT OPERATION

In this study the blood- and fluid-loss caused by operations was measured by four methods: weighing swabs, washing swabs clean and estimating the hæmoglobin in the solution, weighing the patient, and determining blood volumes by the Evans blue method.

For various reasons, the weighing of sponges proved the most useful, though the method usually results in an underestimate. It is pointed out that a bottle of blood is not a pint of blood but 360 c.c. of blood (13 oz.) and 180 c.c. of citrate solution.—A. J. H. Rains: *Brit. J. Surg.*, 43: 191, 1955.

CLINICO-PATHOLOGICAL CONFERENCE. II.

MONTREAL GENERAL HOSPITAL, DECEMBER 15, 1955

TERENCE C. TODD, M.D.
H. ERNEST MacDERMOT, M.D. and
WILLIAM H. MATHEWS, M.D.,
Editors

PROTOCOL

A WHITE HOUSEWIFE, aged 61, admitted on May 24, had complained of pain in the right upper quadrant of the abdomen on and off for about four years. She had been admitted to the Homœopathic Hospital two years previously for diabetes mellitus. Her last attack of severe pain occurred two months before admission, at which time there was x-ray evidence of gallbladder disease. The pain, of a steady, severe boring type, went into the back and up under the shoulder blades. There was no jaundice, and the stools were described as being "light-coloured".

The patient, discovered to be a diabetic two years previously, had been following a diet regularly and taking 25 units of protamine zinc insulin in the morning.

On admission, her temperature was 99° F., pulse rate 76, respiration rate 18, weight 163 lb. She was slightly obese and pale. Her chest was normal, apart from occasional rhonchi. B.P. 142/80. Heart sounds were normal. Nothing abnormal was detected in the abdomen.

Laboratory studies.—The urine, of S.G. 1015, contained a very faint trace of albumin, some white cells, bacteria and epithelial cells on May 25. On May 29, there was no albumin, but 38-40 white cells, bacteria and epithelial cells were still present. The white cell count in the blood was 7,500; Hb 70%. *Stools* were normal. *Blood chemistry:* urea nitrogen 17, sugar (fasting) 181, bilirubin 0.2 mg. % on May 25; sugar (fasting) 158 mg. % on May 27.

Course in Hospital.—The patient was admitted walking, the night of May 24. She was placed on routine diabetic orders and crystalline zinc insulin 10 units in the morning, 10 in the afternoon and 5 at night. Her admission temperature was 99° F., and thereafter—until after operation—the temperature was normal or subnormal.

Two days before operation she was given intravenously 1,000 c.c. 5% dextrose, followed on the next day by a further 2,000 c.c. She was operated upon on the morning of May 29, receiving premedication of morphine, grain 1/6 and hyoscine, grain 1/150.

Operation Report: "Preoperative Diagnosis.—Cholecystitis and cholelithiasis, with associated diabetes. *Operation:* Cholecystectomy, exploration and drainage of the common duct and appendectomy, through a right paramedian incision with hockey-stick curve. The peritoneum was found to be smooth and glistening, and was injected with 1% procaine. The abdomen was carefully explored. No evidence of hiatus hernia; no lesions whatsoever in the greater or lesser curvature of the stomach. The spleen was free; no evidence of any hepatitis in the region of the liver. No thickening of the head, tail or body of the pancreas. Pelvic organs were atrophic.

"Large and small bowel, including the sigmoid and colon, were normal. The appendix, however, was about 9 cm. long by about 1 cm. in diameter, was thickened and injected, and contained three very large fæcaliths. It was resected in the usual manner and the stump invaginated.

"The gallbladder was then examined, and found to contain stones and have a thickened wall; there was a large gland at the neck of the gallbladder and dilatation of the common bile duct. Two-inch packing gauze was

then placed in the foramen of Winslow, and the gallbladder packed off with gauzes. The common duct, cystic duct and cystic artery were dissected free. The common duct was explored below the stump of the cystic. Numerous small mulberry-like stones were washed out of the duct. There was no obstruction into the duodenum.

"A T tube was then sutured into position. Following this, the cystic duct and cystic artery were divided between chronic catgut ligatures and the gallbladder stripped out of the liver bed. A sheath rubber drain was put in Morison's pouch; a sheath rubber drain was brought out through a small stab wound in the right side of the incision. Incision was closed in layers, using No. 2 chromic catgut for the peritoneum and sutures of the same for the anterior rectus sheath. The sheath was reinforced by four figure of eight No. 10 cotton sutures and skin apposition made with No. 10 cotton sutures."

(*Pathological report.*—"Cholelithiasis and chronic cholecystitis. Appendix showed no lesion.")

The patient stood the 2½-hour operation well; the anæsthetic was uneventful, and the condition at close was satisfactory. One hour after operation the B.P. was 70/60 and bile was flowing freely from the T tube. The blood sugar was 153. She was given Pantopon 0.5 c.c. q.4.h. x 72, i.v. 1,000 c.c., 5% glucose saline, and 1,000 c.c. 5% dextrose. Twelve hours later she began perspiring profusely. She slept after sugar by mouth, then perspired again three hours later, was very drowsy and lying with eyes open and staring. Again she improved after sugar *per os*, but said she was not having a reaction. Pulse rapid (140), respiration 40 and B.P. 104/62 (constant).

She was catheterized 19 hours after operation and 1,000 c.c. obtained, and voided 200 c.c. in the same period. Next day, pulse was rapid, irregular and of poor volume, respirations rapid and shallow, colour poor. Very little drainage. Catheterized for residual urine, 80 c.c. obtained. Blood sugar 385.

By 4 p.m. the patient's temperature, which had been normal immediately after operation, had reached 101.8° F. The B.P. was unobtainable, pulse rapid, respirations shallow and rapid. The chest was clear, and no evident reason for the collapse was found. By 6 p.m. the patient was in moderate coma, and there seemed to be sagging of the face to the left. The pupils were equal and not dilated. There was a questionably positive Babinski on the left, with absent deep reflexes. She was not cyanosed, but slightly of a jaundiced hue. There was no abdominal distension or vomiting. No bile drained from the T tube, and she was anuric.

At 7:50 p.m. she was given i.v. 500 c.c. 5% dextrose with 20 units of crystalline insulin. She was placed in an oxygen tent at 8:30 p.m., and died approximately one hour later, i.e. some 30 hours postoperatively.

*Dr. Philip G. Rowe:**

I believe you are all familiar with the history of this case. Briefly, it is that of a 61-year-old woman who complained of intermittent pain in the right upper quadrant for a period of some four years. X-ray examination demonstrated gallbladder disease, but she had never been jaundiced. She was a known diabetic, and for a period of two years had followed a diet and taken protamine zinc insulin each morning.

She was admitted to the hospital on May 24. The examination at that time was essentially negative, though it is important to note that her blood pressure was 142/80. There is nothing to suggest any infective process. Her white count was normal—7,500—and she was afebrile. There were certain abnormal findings, such as an elevated blood sugar of 181 mg. %, slight anæmia with 70% hæmoglobin, and some possible mild infection of the urinary tract. She had 40 white cells in the urine on one occasion.

On the basis of a clinical diagnosis of cholelithiasis, she was operated upon on May 29. The operative findings were as follows: Firstly, the pancreas was not thickened. There was no evidence of hepatitis in the region of the liver. There was no information as to the character of the liver itself, in the way of degenerative changes, such as cirrhosis. There was cholelithiasis, with stones in the common duct. The operation was really an exploration of the common duct and removal of stones therefrom, followed by cholecystectomy and appendectomy.

We are told that the anæsthesia was quite uneventful, and that her immediate postoperative condition was good.

So far the course of events has been clear, and there has been nothing to arouse curiosity; but from this point on, there are unusual features. We note that one hour after operation she had a drop in blood pressure, to a systolic of 70 and a diastolic of 60, with a pulse pressure of only 10 mm. Hg. She was given 2,000 c.c. of intravenous fluids with glucose saline and dextrose. Twelve hours later she perspired profusely; her pulse was quite rapid, 140, but the blood pressure improved to 104/62. The urinary output 19 hours after operation totalled some 1,200 c.c.

Twenty-four hours postoperatively the pulse was still rapid; there was very little drainage, and only 800 c.c. of urine was obtained on catheterization. The blood sugar was elevated to 385 mg. %. Following this, the temperature was found to be 102° F., the pulse still remained very rapid, and the blood pressure became unobtainable. Slight jaundice developed. There was no bile and no urine, and she died within 48 hours.

CAUSES OF DEATH AFTER BILIARY SURGERY

1. Acute pulmonary disease—pneumonia—infarction.
2. Peritonitis.
3. Intracerebral hæmorrhage.

*Surgeon-in-Chief, Montreal General Hospital.

4. Adrenocortical atrophy.
5. Coronary occlusion.
6. Cardiac failure, without coronary occlusion.
7. Hæmorrhage.
8. Liver death—(a) hepatic insufficiency.
   (b) liver shock — hepato-renal syndrome.
9. Lower nephron nephrosis.
10. Acute pancreatitis.

I have listed above a number of causes of death which have in the past been known to follow biliary tract surgery. This list has shown changes over recent years. Formerly it was found that respiratory infections played a considerable role. Peritonitis was another frequent cause of death.

1. *Acute pulmonary disease, including pneumonia and infarction:* In this case there was nothing to suggest an upper respiratory infection, although her respiration became somewhat rapid later on. At that time examination of the lungs was negative, and so I think we are safe in ruling out pulmonary disease as a cause of death. It would be extremely unusual to encounter death within 48 hours from pneumonia following gallbladder disease, and infarction does not follow operation for a period of some seven to eight days.

2. *Peritonitis:* Here again, death from this cause is something which would ensue later. It is extremely uncommon nowadays to find a person dying of this cause after gallbladder surgery. The development of antibiotics has a good deal to do with this, and probably also improved operative technique. This diagnosis can thus be ruled out.

3. *Intracerebral hæmorrhage:* There have been a few cases of this reported as a cause of death after gallbladder surgery, occurring within 48 hours. With this patient, however, there have been no localized signs to suggest an intracerebral accident. It is true she became comatose and had some sagging of the left side of the face, and the deep reflexes were absent towards the end. However, she had no significant changes in an earlier stage, and I think it is reasonable for us to rule this out.

4. *Adrenocortical atrophy,* i.e. subclinical Addison's disease, has been mentioned. It is extremely rare, and I am going to pass over that possibility.

5. *Coronary occlusion* as the cause of death is a possibility; but there is nothing in the symptomatology after operation to suggest such a condition, and the over-all picture does not seem to fit in with a coronary occlusion.

6. *Cardiac failure without coronary occlusion* is becoming increasingly common as a cause of death, because the patients are coming in at a more advanced age, and are more likely to have cardiac damage.

7. *Hæmorrhage* as a cause of death is also a possibility; for example, if the ligature slipped from the cystic duct there would be an intraperitoneal hæmorrhage which would produce shock. Both of these conditions—cardiac failure and hæmorrhage—could result in death if they produced sufficient shock, leading to a condition of (9) *Lower nephron nephrosis,* characterized by first oliguria and later complete anuria, and the patient becoming uræmic. However, death from lower nephron nephrosis is not something you could expect within 48 hours. It might eventuate a week after the onset, but hardly before.

8. *Liver death:* I have indicated this under two headings—hepatic insufficiency and liver shock, or hepato-renal syndrome. Under hepatic insufficiency you will find such conditions as hepatic infection, cirrhosis and necrosis, and certainly we know that in 30% of deaths after gallbladder surgery the cause is hepatic insufficiency. This can be demonstrated by the pathologists. Cirrhosis has been the most common finding, and accounts for possibly 52% of such cases. It is much more common if the biliary disease has been of long standing, say five years or more, and is especially common after biliary tract obstruction or involvement of the common bile duct. However, hepatic insufficiency is not a cause of early postoperative death; the earliest case reported occurred four days postoperatively.

The other condition, liver shock, is a state which was first described by Heyd in 1924. There were a number of cases reported of sudden death after biliary tract surgery, coming on within 48 hours and ascribed to this state of "liver shock". Heyd postulated a state of liver shock as an overwhelming intoxication of liver cells, with vague changes in liver cytology. There has been a good deal of controversy about this, and it has not been entirely accepted. A great many writers have set out their views on the subject. For example, Ravdin would have no part

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of it at all. He felt that this acute liver shock might well be on a basis of liver necrosis following accidental ligation of the right hepatic duct instead of the cystic artery. Others have postulated that it might be on the basis of infection spreading up into the liver and producing a massive infection.

Later on, Heyd introduced the term "hepato-renal syndrome" to include those cases which developed certain renal manifestations, relating to the liver especially; for example, where associated with fever, rapid pulse, decreased secretion of bile, and symptoms of kidney damage with oliguria and anuria. Decidedly, this so-called hepato-renal syndrome is not something peculiar to operations on the gallbladder. In fact, it can follow a number of other conditions—gynæcological operations, severe burns, severe toxic states and poisons. Actually the literature in the last few years has been singularly devoid of cases of deaths ascribed to this so-called hepato-renal syndrome. Many people are sceptical that there is in fact such a condition.

However, in the patient under discussion there are certain things to be considered—the possibility that the hepatic artery might be clamped off, and that the shock which developed, the fever, the suppression of bile, the mild jaundice before death and the associated kidney involvement, such as diminution of urine output and finally the anuria, are all part of the same picture. I think this will have to be considered as a possibility.

The final possibility is the complication of: (10) *Acute pancreatitis.* This as you know is a definite condition which may follow biliary tract surgery, especially where the common bile duct is explored. It may come on very quickly; it may be very fulminating, and may produce death in 48 hours. Patients go into a state of shock quite early. The shock in turn could account for the depression of bile secretion, and also the depression of urinary secretion. It is associated with a rapid pulse, cold clammy skin and much sweating, with high fever and usually with a lot of cerebral depression. The blood sugar is usually quite elevated, as it was in this case. I realize we have no specific data on which to base this possibility, but if I were asked to make a diagnosis I would suggest either a hepato-renal syndrome, which is extremely rare, or acute pancreatitis. I would incline towards the latter, especially because of the fever.

Dr. Todd:

Dr. Mills, would you care to comment on this case?

*Dr. Edward S. Mills:**

I am not sure that I agree with Dr. Rowe. I have reviewed all the suggested diagnoses in my own mind in the last few days. First I was inclined to diagnose liver death, but the patient died, I observe, within 30 hours of operation, too rapidly for this condition. What is more, over 1,200 c.c. of urine were voided in the first few hours after the operation. So there was no renal shut-down during this period—not until the final hours. Therefore I am inclined to rule out the hepato-renal syndrome.

Consideration should be given to other conditions which can produce sudden death—for instance, an intracranial lesion, but at no time were there symptoms referable to the nervous system. Dr. Rowe mentioned massive coronary occlusion, but the patient showed no evidence of acute pain. It should be noted that her blood pressure fell suddenly during operation and then came up and remained fairly constant for a period of time; then it went down and she became anuric. There is a rather rare condition which occurs sometimes in meningitis and sometimes in pregnancy: bilateral hæmorrhage into the adrenals—the Waterhouse-Friderichsen syndrome. This would account for the sudden drop in pressure and death within 24 hours. It is more likely to produce death in such a short time than is liver necrosis or even pancreatitis. I think lower nephron nephrosis can certainly be excluded, by reason of the good renal function in the first 18 hours of the postoperative period. I would favour a diagnosis of Waterhouse-Friderichsen syndrome.

Dr. Todd:

Dr. Joron, would you comment on this case from the diabetic viewpoint? What do you think of the possibility of infection?

Dr. Guy E. Joron:†

It is not uncommon to find that an operation in itself causes increased resistance to insulin. This

*Physician-in-Chief, Montreal General Hospital.
†Assistant, Department of Metabolism, Montreal General Hospital.

may have accounted for this patient's high blood sugar level. Had she had a Waterhouse-Friderichsen syndrome I think she might not have had a similar rise.

From the diabetic point of view I think we have to consider the possibility of acute pyelonephritis. This is a common complication of diabetes, and there was some evidence that she had a urinary tract infection. We are not told whether the urine examinations were done on voided or catheter specimens. The patient was catheterized postoperatively, which in itself may have stirred up trouble. Certainly we have to recognize that an acute pyelonephritis could cause this type of death, and I think this should be added to the differential diagnosis.

*Dr. Joseph E. Pritchard:**

In connection with liver shock, I would like to draw attention to a few cases of what might have been called sudden death after cholecystectomy, and one in particular in which death occurred within ten hours. In that case there was a very marked biliary tract obstruction, with jaundice and dilated gallbladder and common duct. At autopsy, the liver was what one can only call shattered; there were multiple hæmorrhages throughout the whole of the organ, and the whole liver structure seemed to be blown apart. At that time, I believe this was one of the things that was included under "liver shock". I have not seen any such cases recently, and the one I mention in particular occurred about 30 years ago. I see that in the present case there was slight jaundice, which points to the possibility of a similar condition.

Dr. Todd:

Both Dr. Mathews and I agreed that this case was probably impossible to diagnose correctly. It was taken from the autopsy records of the year 1946, and was selected as an exercise in the differential diagnosis of death postoperatively.

Clinical Diagnosis:
Cerebrovascular accident?
Hepato-renal syndrome?

Dr. Philip G. Rowe's Diagnosis:
1. Acute pancreatitis
2. Hepato-renal syndrome.

Pathological Diagnosis:
Gas gangrene — *Clostridium perfringens (welchii).*

DISCUSSION OF PATHOLOGY

Dr. Mathews:

At post-mortem examination, the salient features were the demonstration of a soft friability and pallor of the muscles in the vicinity of the right paramedian operative wound together with crepitations and visible bubbles in the surrounding fat which had been liquefied. The venous blood was dark, liquid, and contained bubbles. The bubbles were present throughout the serous membranes and in the subarachnoid space. The parenchymatous organs likewise revealed bubbles of gas formation and acute degenerative swelling. The operative fields were in no way remarkable or abnormal, save for the changes in the wound of the abdominal wall.

These gross appearances consistent with a clostridial septicæmia were confirmed by the isolation of *Clostridium perfringens* from the blood. There were no other pathological lesions pertinent to the death.

The microscopic sections demonstrated the necrosis and œdema of the muscle of the abdominal wound and the large numbers of bacilli that were present, and the liver degeneration with gas bubble formation wherein there again were seen swarms of the bacilli.

Dr. Todd:

Dr. Pretty, you operated on this patient. Would you care to comment?

*Dr. H. Gurth Pretty:**

I must admit that I was as baffled by the immediate postoperative situation as were Drs. Rowe and Mills.

The interesting point was this: On exploring the abdomen, a very unusual looking appendix was found, and I made definite note of it. Instead of the average appearance of an appendix, this was sausage-shaped, had a dusky redness about it and was œdematous. But after it had been removed and the stump tucked in, there was no danger of swelling. I did not notice at the time whether any large glands were apparent in the mesentery.

*Pathologist-in-Chief, Montreal General Hospital.

*Hon. Attending Surgeon, Montreal General Hospital.

The other noticeable postoperative point was the immediate drop in blood pressure. At about that time a patient's blood pressure is likely to vary, in the process of his being taken through the surgical procedure and from the operating table to the bed. An immediate drop needs to be counteracted. Subsequently the pressure rose nearer to the normal. During the immediate postoperative course, we noticed a very rapid rise in temperature, which led us to suspect collapse of the lung. It did not fit into the picture. Then the patient gradually went on and, instead of improving, entered into a general collapse. I thought she had died of a cerebrovascular accident or hepato-renal syndrome, because afterwards when we tried to palpate the abdominal wall we did not get any suggestion of gas. The only suggestion we could make was a possible collection of organisms of the gas-gangrene bacillus type in and around the appendix rather than the rest of the bowel. The removal of the appendix must have opened up the lymphatic spread and caused a generalized septicæmia, as in a pylephlebitis.

One other interesting feature is that this is the third case of gas-gangrene bacillus death I have seen following appendectomy. There are several other cases of deaths on record due to this cause, but they did not come on quite as rapidly as this one.

Dr. Todd:

Dr. de Vries, would you say something about the bacteriology of gas gangrene?

*Dr. Joan de Vries:**

This case is more interesting from an historical point of view, because we do not encounter this type of incident any more, especially since the beginning of the use of penicillin. It is very rarely that we isolate this organism at all from any source, so septicæmia caused thereby is extremely rare. For instance, the uterus must often be contaminated with *Cl. perfringens* in an infected abortion, yet gas gangrene does not occur because of the routine administration of penicillin in cases of this type.

I think it is very interesting, because as you know there is a movement to do away with, or cut down, the routine administration of penicillin postoperatively, and I think the case under review causes one to pause and reflect.

I believe that no blood cultures were taken. They would have been of little use, because they would probably not have shown positive results before the patient's death. If it can be stated, I would like to know the source of infection. I am not sure that it was the appendix—but this is a point which probably cannot be definitely determined.

Dr. Todd:

Dr. Pretty thinks the appendix was the most likely source of infection.

Dr. Mills:

I would like to ask the pathologist whether it is usual for a person to die of gas-gangrene infection within 18 to 30 hours. Has he seen other cases like this?

Dr. Pritchard:

I have seen some cases in which death occurred very quickly. I am not certain about the exact time, but necrotizing pancreatitis, for instance, associated with *Cl. welchii,* has brought about early fatal results. Whether the infection was the cause or not, I don't know. In this present case the gas would be exaggerated in the tissues because the organisms would keep on producing gas after death. In my experience, some patients with gas gangrene die very quickly—this applied particularly to war wound infections. One patient who was admitted feeling reasonably well was dead the next day, with an overwhelming infection.

Dr. de Vries:

This organism produces three toxins, one of which is very lethal, and death can occur in a matter of hours with very small amounts of this toxin.

Dr. Todd:

I believe it is very rare to get a *Cl. welchii* infection by itself; is there not usually a mixture of organisms?

Dr. de Vries:

Gas-gangrene of muscle following wound infection is usually mixed, but septicæmia is usually due to one organism.

*Bacteriologist, Montreal General Hospital.

Clinical and Laboratory Notes

A PHYSICIAN'S SUBJECTIVE IMPRESSIONS OF MODIFIED INSULIN THERAPY*

MILO TYNDEL, M.D., Ph.D.,
Brandon, Man.

THE CLINICAL PICTURE of hypoglycæmia is well known and many diabetic patients have reported on their subjective experiences during hypoglycæmic states. There are also reports by psychotic patients on remission or recovery of the psychosis. So far as I know, however, there have been no reports by a non-psychotic physician on his subjective experiences during sub-coma therapy.

The patient was a well-qualified physician, 32 years of age, but of an unstable, inadequate personality who presented the clinical picture of an anxiety state with some obsessive features and addiction to phenobarbitone. Several psychotherapeutic attempts had been followed by relapse.

An asthenic type to start with, he had become emaciated, and modified insulin therapy seemed indicated. Treatment was given in an insulin therapy unit with doses of up to 100 units daily. He accepted the treatment readily, improved physically and psychologically, and willingly gave the following account of his experiences. It is reproduced in his own words, and shows not only the physiological—essentially vegetative—changes experienced, but also the psychological effects, notably the aggression aroused during the phase of excitation.

IMPRESSIONS OF MODIFIED INSULIN THERAPY

"I have now been on insulin therapy for two weeks. The following comprises the subjective symptoms I have experienced to date. Approximately one-half hour after receiving insulin I notice that my face becomes somewhat warmer; my hands become warm and dry with paræsthesiæ in the form of a tingling sensation in the palms; my feet are cold; I begin to feel very relaxed and calm. I soon fall asleep. After one hour I awaken, to find that my hair, brow, face and neck are covered with perspiration. My heart is beating very strongly; the pounding appears to be so intense that it would seem as if it would not take much to force the apex of the heart through the thoracic cage. This pounding of the heart, together with the numerous extrasystoles which occur, makes me very uncomfortable indeed and extremely restless, so that I toss from one side to the other in the bed. The amount of sensible perspiration increases greatly and soon I feel myself to be bathed in sweat. For some inexplicable reason I become angry and feel very hostile towards doctors, nurses, attendants, and towards the other patients in the ward. Moreover, I feel belligerent, having the idea that I would like to 'take on' the doctors and the attendants in a fist-fight. This phase lasts about one-half hour, by the end of which time the forceful heart beating has subsided, perspiration has decreased in amount, my feeling of animosity has departed. I have a feeling of tranquillity and again fall asleep.

"I now sleep uninterruptedly for another hour, at the end of which time I am awakened by a nurse; I ingest the sugar solution, and again fall asleep. At the end of half an hour I awake at the attendant's call or touch and rise out of bed.

"After awakening I feel moderately thirsty and extremely hungry; I no longer feel tired. I notice that I have a gross tremor of the hands. This tremor diminishes gradually during the day, is still present at bedtime, and is gone by the following morning. Also, I notice that, as the day progresses, I become less apprehensive and more relaxed. By the time evening rolls around I feel carefree. I sleep well, although I am disturbed twice by nocturia (it may be noted that before starting insulin therapy I had never had to get up at night to urinate). I arise the next morning feeling very happy, thinking that I would like to sing and dance. I proceed again to insulin therapy and the cycle is begun anew."

I am indebted to Dr. Stuart Schultz, Medical Superintendent, Hospital for Mental Diseases, Brandon, for permission to publish this paper.

*From the Hospital for Mental Diseases, Brandon.

BENIGN ULCERATION ON THE GREATER CURVATURE OF THE STOMACH

Ulcers on the greater curvature of the stomach are generally malignant lesions but many recent reports suggest that benign ulceration in this region is not as rare as it is generally considered to be. Of 148 surgically resected and microscopically verified benign gastric ulcers, encountered between 1948 and 1954 at the Ochsner Clinic and Ochsner Foundation Hospital, seven (5%) were found on the greater curvature.

Adequate roentgenological examination is the most available, the easiest, and probably the most accurate means of differentiating between benign and malignant gastric lesions. While benign ulceration of the greater curvature of the stomach is being reported with increasing frequency, the radiologist and clinician must remain aware of the fact that the vast majority of ulcers in this area are malignant in nature.—S. Ochsner: *Am. J. Roentgenol.*, 75: 312, 1956.

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Editor: S. S. B. GILDER, T.D., M.B., B.Sc.

Managing Editor: T. C. ROUTLEY, M.D., F.R.C.P.[C.]

Consultant Editor: H. E. MACDERMOT, M.D., F.R.C.P.[C.]

Editorial Offices: 150 ST. GEORGE ST., TORONTO

(Information regarding contributions and advertising will be found on the second page following the reading material.)

RABIES IN CANADA

The present enzootic of rabies is the most extensive that Canada has ever experienced. It began in the Northwest Territories and has extended to northern British Columbia, almost all of Alberta, the northern parts of Saskatchewan and Manitoba, the greater part of Ontario and parts of Quebec and Newfoundland. Whereas all outbreaks in the earlier part of the century had been confined to the older settled parts of Canada, and involved domesticated animals, this present enzootic involves the wildlife population and, in particular, foxes and wolves.

The first proven outbreaks of rabies occurred in Canada in 1907 and, although they were quickly suppressed in Manitoba and Saskatchewan, the outbreak in the Niagara Peninsula in Ontario continued for some ten years.[1] During this period many people were bitten by rabid dogs; in addition, horses, cattle, sheep and swine contracted the disease. Rabies again appeared in 1926 in lower Quebec and spread to Montreal and the Gatineau and Ottawa Valleys in Ontario and Quebec. In 1928 it appeared in scattered foci in Ontario including Windsor, the Niagara district and Kingston. It was eradicated in 1931. The Windsor district was again involved during 1944-47. There have been a few other scattered foci of infection.[2, 3] In all these outbreaks, the disease occurred only in domesticated animals and principally in dogs.

According to Plummer,[4] the history of the present outbreak probably goes back to the late 19th century, originating in a condition described in sleigh dogs and wild animals as affecting the central nervous system. It was not until 1947 that the diagnosis of rabies was confirmed in a fox and a dog at Baker Lake, some 400 miles north of Fort Churchill in the Northwest Territories. By 1952 it became evident that the disease was enzootic throughout the Northwest Territories and was extending southwards. Alberta was invaded to a greater extent than the other western provinces. Infected animals were found in all parts of the province except in a narrow strip along the international border. In early 1953 rabies was found in dogs and foxes in East Maine, Quebec, on the east shore of James Bay. Further cases were found in northern Quebec and Ontario in 1954, and by the end of 1955 the enzootic had spread throughout the north-eastern portion of Ontario and extended far southwards. Up to the present, infected animals have been found in most parts of Ontario except for a small area in the south-eastern portion and a few counties in western Ontario.

One of the interesting features of this enzootic is the fact that although some domestic animals such as dogs, cats, cows, pigs and sheep have been involved, the greatest proportion of infection has been in wild animals. Evidence suggests that the fox is the most dangerous reservoir. This makes the problem of control rather more involved than heretofore when measures were adopted to eradicate the disease in the dog population.

Efforts have been made through the Department of Agriculture, Health of Animals Branch, with the co-operation of the Provinces to restrict the enzootic by: (a) reducing the wildlife population, which in the case of foxes seems to have increased; (b) restricting the movement of dogs; and (c) immunizing domestic animals.

Following the evidence presented by Koprowski[5, 6] that a modified live virus vaccine, grown in the developing chick embryo, could produce a solid and lasting immunity in animals following a single dose, a simple and effective means of preventing rabies in domestic animals became available. This is not only important from the standpoint of preventing transmission of rabies to humans from household pets but is of economic importance to farmers in reducing losses in livestock. This type of vaccine has not yet been approved for human use. An effective programme of enforcing registration of dogs and cats and restricting their movements will further reduce the hazard of human infection from these sources. In addition, an active programme of

public education cautioning children and adults alike to avoid wild animals that show signs of illness or any peculiar behaviour including apparent tameness, dead animals and unknown or stray dogs is indicated.

The physician is constantly faced with dog and cat bites, not only as a surgical problem but with the possibility of infection with rabies virus. In the immediate treatment of the wound, it is well to consider tetanus prophylaxis either with toxoid in those who have been previously immunized, or with antitoxin in those who have not received toxoid before or where the previous history of immunization is uncertain. The use of fuming nitric acid, traditionally recommended for cauterization of wounds inflicted by animals suspected of harbouring rabies virus, has been generally abandoned. Experimental evidence has shown that thorough irrigation with 20% soap solution or with 1% Zephiran solution is as effective and leaves less scarring.[7] Thorough treatment of the wound is more effective when carried out within two hours after the bite than after six hours.

While the phenolized or Semple type vaccine has been used generally in the treatment of persons bitten by rabid animals and, in certain large series of cases, has been shown to save four out of every five persons who would otherwise develop rabies and die, it has certain disadvantages. In cases where there have been severe and extensive bites about the head and neck, and where the incubation period may be less than 3-4 weeks, its effectiveness is doubtful. Further, the treatment must be early and adequate. It is a major undertaking since at least 14 daily injections are required. While post-treatment complications are not common they may be severe, varying from paralysis due to a peripheral neuritis, to dorsolumbar myelitis and acute ascending myelitis of the Landry type. Only one neuroparalytic accident has been observed recently in Canada. While every effort must be made to ensure early and adequate treatment for those who require it, the indications must be weighed carefully and the treatment with vaccine not undertaken lightly.

Recent evidence indicates that a hyperimmune antirabies serum, administered early and used in conjunction with the vaccine, may be of benefit in those cases where exposure has been severe and where the incubation period might be short.[8]

R. J. WILSON

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REACTIONS TO ANTIHYPERTENSIVE AGENTS

In this modern age of chemotherapy, a substantial price in undesirable side-effects is being paid by many patients for the actual or presumed beneficial properties of the newer drugs. This state of affairs is not new, however, since adverse reactions to drugs have been known since the early days of chemotherapy. Mercurial and arsenical preparations used in the treatment of syphilis produced stomatitis, hepatic disease and exfoliative dermatitis. Certain older analgesics containing the benzene ring caused bone-marrow depression, and history is now repeating itself in the case of phenylbutazone. More recently, a complete series of precautions was necessary for the safe administration of sulfonamides, to prevent urinary obstruction and hæmopoietic disorders. With the advent of antibiotics it was hoped that an era of non-toxic antimicrobial therapy had finally dawned. But anaphylactic deaths from penicillin continue to be reported in the literature; streptomycin has harmful effects on the auditory nerve and the kidneys; the tetracycline compounds cause nausea, vomiting and diarrhœa; and chloramphenicol has been implicated in numerous reports of bone-marrow depression following its use. This state of affairs has recently received attention in a very thoughtful article by Barr,[1] in which the undesirable side-effects of diagnostic and therapeutic agents are reviewed.

During the past few years there has been an intense interest in antihypertensive drugs, and one after another has appeared on the market, all with high claims of effectiveness, and few with any emphasis on toxicity. However, these hypotensive drugs have been found, after wide usage, to present the same disadvantages as did the earlier chemotherapeutic agents. The original examples of this group—the veratrum alkaloids—have, as an integral part of their pharmacological

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effect, so intense an emetic action that no dosage schedule can be devised that will at the same time exploit their hypotensive effect and restrain their emetic propensities; and no chemical modification of these alkaloids devised with this end in view has met with any substantial degree of success. The tetraethylammonium and pentolinium compounds show no specificity in their ganglion-blockading effects, and the treatment of hypertension with these agents results in gastrointestinal and vesical atony in a high percentage of patients. Finally, one of the most bizarre of syndromes results from the administration of the hydralazine group, in which practically all the features of systemic lupus erythematosus, and possibly other collagen diseases, are mimicked.

Until recently, however, it appeared that the various members of the Rauwolfia group could be prescribed with impunity in the treatment of essential hypertension; and that, even though their hypotensive effect was modest, patients would suffer only minor irritating side-effects such as nasal stuffiness and occasional diarrhœa. However, it now appears that even these presumably innocuous preparations cannot be used with any more freedom than has been the case with the more potent antihypertensives. In this issue (page 522) Lemieux, Davignon and Genest draw attention to undesirable side-effects of a modern antihypertensive agent. This has also been noted elsewhere. Freis,[2] more than a year ago, reported five cases of mental depression in hypertensive patients treated with reserpine. All these patients exhibited withdrawal, lethargy and unhappiness; some complained of lack of ambition, crying spells and introspection; and two actually contemplated suicide. Fortunately, the symptoms cleared in all but one of the patients soon after the reserpine was discontinued; *but* one of these depressive psychoses actually terminated in suicide. Since that report, others along similar lines have appeared in the literature. Muller *et al.*[3] recently reported a severe mental illness occurring in seven of ninety-three patients receiving Rauwolfia preparations for periods of two to twelve months. The mood disturbance was primarily depression in two patients, depression with anxiety in three, and an anxiety state in two. Suicidal tendencies were present in two patients. The severity of this complication is attested by the fact that, although the drug was discontinued, only two of the seven patients responded to reassurance and supportive treatment, while five required electroconvulsive therapy. Previous psychiatric illness had been present in five of the patients.

Concurrently, Schroeder and Perry[4] have reported the development of psychotic states in five patients taking reserpine preparations. These included nervousness, insomnia, agitation, depression, and paranoia with suicidal tendencies. Although the drug was discontinued, recovery was slow and required one or two months. Non-psychiatric complications resulting from the peripheral autonomic effects (relative parasympathetic stimulation) of reserpine are also mentioned, including recurrence of peptic ulcer with bleeding, and severe mucous colitis.

In the same issue of the same journal, in reporting a controlled study of fifty-eight hypertensive patients treated with crude Rauwolfia preparations and reserpine, Achor *et al.*[5] have this to say, "The most disturbing and unexpected observation to come out of this study is the frequency with which mental depressive states developed (10 of 58 patients). This effect has been noted by others, but the severity to which symptoms can progress has not been sufficiently stressed . . . it is our present belief that *Rauwolfia serpentina* increases the vulnerability of . . . susceptible persons to factors in their environment that may promote a depressive response. We believe that the seriousness and frequency of these reactions constitute a major contraindication to the indiscriminate and unsupervised use of Rauwolfia preparations in persons with essential hypertension." Similar sentiments have more recently been echoed by Kass and Brown,[6] who, in a three-month period, saw four patients treated with Rauwolfia compounds and reserpine, in whom these preparations had precipitated mental depressions, in one case amounting to a psychosis.

All these workers emphasize, and the present writer agrees, that *Rauwolfia serpentina* and reserpine, despite these recently documented disadvantages, represent a most valuable adjunct, if not the keystone, in the present-day therapy of essential hypertension. Nevertheless, as with all chemotherapeutic agents, their use is not without its dangers; and, with this new information at hand, the wise physician will undoubtedly screen his hypertensive patients most carefully before prescribing these preparations in the future.

S.J.S.

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Editorial Comments

CONVENTION EXPENSES RECOGNIZED

In his Budget Speech delivered to Parliament on the evening of March 20, the Honourable Mr. Harris, Minister of Finance, used the following words:

"Members of the professions and others who have been affected by a recent Exchequer Court decision which ruled out a deduction for convention expenses, will doubtless be interested in learning that the Act will be amended to allow for 1955 and onward, the deduction of expenses for two conventions annually in Canada."

Although the exact terms of the amendment and any regulations which may be promulgated are not yet available, the forecast quoted above will be received with some satisfaction by practising physicians. Following adverse decisions by the Income Tax Appeal Board and the Exchequer Court of Canada, the Income Tax Committee of The Canadian Medical Association made the strongest efforts to achieve an amendment of the Income Tax Act to permit the expenses of attending medical meetings to be recognized as properly deductible expenses of practice.

Although the proposed amendment does not cover the expenses of attending meetings outside Canada as we hoped it would, the current proposal is to be regarded as the recognition of an important principle. Although a touchdown may not have been scored on this play, important yards have been gained. The C.M.A. was the ball carrier in this instance, assisted by valuable blocking provided by the Canadian Dental Association. The health professions, whose conventions provide the opportunity to learn and to teach, are, with the public whom they serve, the chief beneficiaries of the proposed amendment.

Certificates of attendance at the 1955 Conjoint Annual Meeting of the B.M.A.-C.M.A.-O.M.A. were distributed to Canadian doctors who attended with the advice that a claim be made for expenses despite the uncertainties which then surrounded the whole subject. The Minister's announcement that the amendment will be retroactive to the taxation year 1955 has justified this advice.

Although modified rapture may appropriately describe our initial feelings, all members of the medical profession will recognize that an important principle has been established and we have learned in the process that soundly based recommendations to the Ministers of the Crown are often translated into good law. A.D.K.

THE PROGNOSTIC VALUE OF LIFE INSURANCE MORTALITY INVESTIGATIONS

Research and academic and clinical medicine have not realized to the full the wealth of statistical information on both health and disease which is to be found in insurance statistics. The vast number of cases in joint inter-company studies makes them statistically reliable and worthy of careful study along with other statistical information.

Recently the Society of Actuaries in consultation with the Association of Life Insurance Medical Directors of America published the results of a joint inter-company life insurance mortality investigation of persons with histories of various diseases and impairments, under the title of "The 1951 Impairment Study". This study, covering some 25,000 lives, is the latest and most comprehensive of a series of life insurance mortality investigations. The findings in certain of the more important diseases were presented in graphic form on charts and were first shown in a scientific exhibit at the Annual Meeting of the American Medical Association at Atlantic City in June 1955 and later in the same month at the Conjoint B.M.A., C.M.A., O.M.A. Meeting in Toronto. The charts aroused much interest on the part of the profession, and as a result the Professional and Public Relations Committee of the Association of Life Insurance Medical Directors has now published them in the form of a booklet.

This booklet aims: (1) to present facts on prognosis in persons with histories of various diseases or impairments; and (2) to acquaint physicians with an important source of information on prognosis.

The charts in this booklet compare the survivorship record over a 15-year period of persons with selected impairments or histories, with the corresponding record of persons insured at standard premium rates. Also shown in the charts are the ratios of the actual mortality experienced among the impaired lives to that among persons insured at standard premium rates. Attention is further drawn to some of the major factors that have influenced the results and to the major causes of death responsible for the excess mortality.

The persons whose survivorship record was followed in the "1951 Impairment Study" were accepted for insurance under ordinary policies in 1935-1949 and were traced through 1950. They were all medically examined and had no significant impairment other than that which was being investigated. In interpreting the findings, it must be remembered that the entrants in many groups were very carefully selected. Frequently only the best cases were accepted for insurance, while those with complications or not in good health were declined.

As a public relations service, the Association of Life Insurance Directors of America is cur-

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rently mailing a copy of this booklet to (1) fellows of the American College of Physicians; (2) certified specialists in medicine and in public health of the Royal College of Physicians and Surgeons of Canada; (3) deans of each medical school in the United States and Canada; (4) hospitals with 100 or more beds, medical libraries and health officers in each large city in both Canada and the U.S.

Any physician not included in the above may receive a copy on request to Dr. C. D. Gossage, 321 Bloor Street East, Toronto.

NEEDLE BIOPSY OF THE KIDNEY

Kidney biopsy is one of the more recent adjuncts to medical diagnosis in renal disease. This technique as a percutaneous procedure was first used by Iversen and Brun.[1] In their hands only about 38% of biopsies were successful, excluding the test as a reliable clinical tool.

In 1954 Kark and Muehrcke[2] devised a new method using a modified Vim-Silverman needle, with the patient in the prone position. Their results were apparently successful in 93% of patients.[3-5] These authors also improved their results by localizing the kidney accurately with a preceding x-ray examination.

It is advisable when attempting this procedure to limit the operation to the right kidney where possible, the left being in a more vulnerable position with the spleen and large vessels in the immediate locality. After the surface markings of the lower outer pole of the right kidney have been determined radiologically, a thin exploring needle is inserted at the site to find the depth of the kidney from the surface. This is determined when the exploring needle moves in an anteroposterior arch synchronous with respiration and the movement of the kidney. The depth and direction having been determined in this manner, the modified Vim-Silverman needle is introduced and used according to the instructions supplied with the needle.* The usual biopsy specimen obtained is about 10 mm. in length and the diameter of a 17 gauge needle. The specimen is best fixed in 10% formalin. After completion of the biopsy, the patient is kept in a prone position with pressure at the biopsy site for about 20 minutes, and carefully observed for any complications for the next six hours.

Before a needle biopsy is attempted, one should be certain that there is no bleeding tendency, or a non-functioning opposite kidney. Pyonephrosis, hydronephrosis, and uræmia are contraindications to carrying out the procedure.

Transient hæmaturia, either macroscopic or microscopic, is common and not usually serious. Because of the firm renal capsule this procedure will likely prove to be as safe as or safer than liver biopsy. The latter carries a mortality of about 0.3%.[6]

With the possible risk in mind, it is obvious that renal biopsy should only be done where there is adequate justification; this usually means that the patient will possibly derive some benefit from the procedure.

The examination will be helpful in correlating physical findings with the pathological picture and the laboratory tests, leading to a better understanding of renal disease.

It is also possible with this technique to culture a portion of the biopsy core which will give a specific cultural diagnosis. This will make it possible to give the appropriate antibiotic, especially in those cases where many organisms are cultured from specimens obtained from the lower urinary tract.

Renal biopsy, it thus can be seen, is at present useful only in clinical investigation and then only when the patient might benefit by it. It is useful in making a specific diagnosis on undiagnosed types of clinical renal disease, in order that rational therapy can be instituted and the prognosis determined.

It is not likely that renal biopsy will ever become a routine procedure, but if utilized properly it can be a useful tool in diagnosis and treatment, and from it can be learned a lot of information regarding the intermediate phases of renal disease.

G. W. SMITH

*Vim-Silverman Needle, McGregor Instrument Co.

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THE PRESSES ROLL

Three official publications of the Canadian Medical Association have recently been received from the printers. Each of them represents the product of months or years of effort by committees, as well as painstaking work by the staff in preparing them in final form. The new publications and their distribution are as follows:

"You and the C.M.A."—an illustrated brochure for members of the medical profession to acquaint them with the operation of the Association. Distribution will be made by mail according to the instructions of the Divisions. A version in French will shortly be available.

"The Code of Ethics," revised 1956. Copies are available to individuals, medical schools and related organizations, on application to the General Secretary.

"Basis of Approval of Hospitals for the Training of Interns in Canada." Distribution will be made to eligible hospitals with new application-for-approval forms. Chairmen of Intern Committees and other interested physicians may obtain copies from the General Secretary.

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PUBLIC RELATIONS FORUM

Conducted by L. W. HOLMES
Assistant Secretary, C.M.A.

XIV. MEDICINE ON THE AIR

RADIO AND TELEVISION are two media of mass communications little used by the medical profession for health education and improvement of public relations. This, despite two facts: (1) organized medicine, in its Code of Ethics, considers it "legitimate and even desirable that topics relating both to medical science and policy, and to public health and welfare, should be discussed by physicians who can speak with authority on the question at issue"; and (2) radio and TV are two of the most effective means of informing and educating. In this article, radio, the older of the two media, will be discussed.

One would find it most difficult, if not altogether impossible, to assess the influence of radio as a social instrument. Despite the momentous growth of television in Canadian life, radio has not been replaced; its place in the home has only been altered. Instead of being the centre of home entertainment, it has become the companion of the kitchen, the bedside, the den and desk, wherever the hands are busy and the concentration necessary to viewing is undesirable. Its role in entertainment on the highway grows in importance.

In this change, radio has not lost any of its values. Though a mass medium, it still possesses the qualities of a direct personal touch as it uses the spoken word, for the most part, to convey its message. The spoken word can be more compelling that the printed word; it can be more personal, more friendly, more timely. In other words, radio has the qualities of immediacy and intimacy. These are the qualities which make radio effective as a medium for health education.

As is well known, Canada has a unique radio system. It combines a network of state-owned radio stations with privately owned stations which act independently of and as outlets for the network. There are more than 145 privately owned stations in Canada; these represent the best market for organized medicine.

In most instances, medical societies can secure public service time from radio stations for airing medical programmes. This means that the time will be provided free of charge to the society. Of necessity, establishing good radio relations is as important to a medical society as building good press relations. Moreover, it is necessary to present a programme which will further the aims of the radio station—public service, yes, but, more important, the winning of listeners. Realistically, few radio stations are going to co-operate with medical societies because they believe they morally should do so. Radio stations, like instruments of other media, exist because they are economically and competitively sound. This requires good programming. Consequently, the medical society planning a radio series must have good programme ideas and personnel who can and will participate, and must be prepared to "sell" the ideas to the station managers.

To ensure programming within absolute control of the medical society, and at a time of day guaranteeing listenership, purchase of radio time may be necessary. This is the policy followed by the British Columbia Division of the C.M.A. For the cost of $83 a week the Division is able to buy 15 minutes of radio time plus the service of a scriptwriter, announcer-interviewer. It is estimated that this weekly programme reaches 9,000 listening homes in Greater Vancouver.

It is also possible to produce health education programmes in co-operation with other organizations. For example, the medical society might co-operate with a city hospital, city health department, Blue Cross, or such organizations as the local cancer society, in airing a programme. Or the society may be able to obtain time on an already scheduled women's programme or other regular feature to present medical information.

Medical programmes get on the air in one of two ways. The radio station may approach the local medical society requesting assistance in preparation and presentation of health education. Or the medical society may decide that it should approach the radio station for radio time as part of its public relations programme. If the latter should be the case, the society should stress the need for the programme and the excellence of the broadcasts planned. Should the radio official contacted reject the programme ideas advanced but make alternative suggestions, it is wise to listen to him. It is an indication that he is interested and, with his background of radio experience, he is in a position to approach radio programming more realistically, and with greater assurance of success.

If, on the other hand, a representative of a radio station should approach the society for assistance, he should be received courteously and his overtures listened to. Co-operation, if at all possible, should be given in the interest of furthering good public relations and of meeting the need for accurate health information. The type of programme satisfactory to all parties can be arrived at in further discussions.

What type of programme should the medical society produce? There are five basic types: the talk, the interview, the roundtable or panel, the documentary, and the dramatization. The first, by far the simplest, is unfortunately the least attractive from the listener's point of view. The interview is probably the next in ease of production and has proven far superior in holding listener attention. The roundtable, providing still greater variety of voice and idea, is worthy of consideration. The last two types, the documentary and the dramatization, will probably prove to be beyond the resources of both society and

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radio station. The type which the society considers will depend on just that—the resources of the doctors and the radio stations; the personnel, the material, the time. If the radio station can provide a staff member as interviewer, perhaps the most satisfactory programme type in terms of interest, cost and effort will be the interview.

Another consideration is the series vs. one-shot production. Certainly the radio series, at a fixed time and following a particular theme, is the better of the two approaches. The single programme approach is adequate if there is a particular message which the society wishes to get to the public. But, from the point of view of public relations, the series should be seriously considered. Series programming is usually built in multiples of 13 shows. The most common is 26 weekly shows to the series.

The subject matter, which, of course, will be essentially educational, should be chosen with three objectives in mind: adaptability for radio, personnel, and suitability. Most common medical topics are adaptable for radio discussion. Personnel can usually be found who can adequately handle the topic at issue. The third factor depends on whether the time is purchased or donated. If the latter, controversial subjects should be avoided. Of course, the content need not be limited to clinical subjects. Doctors could very profitably discuss such topics as emergency call systems, mediation committees, the desirability of each family's having a family doctor, and similar matters.

There are two schools of thought on the question of personnel, one representing the approach of the society, the other the point of view of the radio station. The medical society usually requires that a different doctor appear on each programme. The station, on the other hand, would prefer to have the same doctor appear throughout the entire series; such an approach usually ensures having a doctor who has a satisfactory radio voice, and who requires little further training in the ways of radio after the first programme or two. At the same time, the listener begins to associate the voice with the series. The medical society can justify either approach. Medical ethics, which oppose advertising in any form, can be cited as the reason for using different doctors; on the other hand, the Code of Ethics permits the society to request a doctor to speak on its behalf, with no limitation as to time or occasions. Perhaps the most satisfactory arrangement is the utilization of a non-practising physician—a health officer, a member of a university staff—throughout an entire series of programmes.

The interviewer, if the interview type of programme is employed, should be a member of the radio staff, someone familiar with radio and all its complex ways, one who is adept at proper organization of thought and material, and who can develop the interview logically.

At some time or other medical societies experimenting with radio have had to face the question: Should the doctor participating be identified? The answer is found in the Code of Ethics under a discussion of radio broadcasting. "In any medium of discussion," the Code reads, "but especially in radio broadcasting because of its vast range, it is essential that the physician who takes part should avoid methods which tend to his personal professional advantage. Not only should he personally observe this rule, but he should take care that the announcer in introducing him makes no laudatory comments or unnecessary display of the physician's medical qualifications and appointments."

In that section, the Code, by omission, suggests that the doctor may be identified by name. Certainly, identification is desirable. People require authority for what they are told. This is as true of radio as it is of the newspaper. An anonymous voice lacks much of the conviction possessed by Dr. So-and So, who is known, either personally or by reputation.

The final step in placing medicine on the air is promotion. Like the health forum and the speakers' bureau, the radio series must be publicized. Leaving the listenership to chance, in these days of dial twisting, is highly unscientific. Frequently the radio station will provide assistance. With or without this help, the medical society should use every device at its disposal to tell potential listeners about the series, and on a continuing basis, about each individual programme.

Next article: the most recent, most interesting and useful medium to come upon the mass communications scene—television.

PR TIP

Dr. Paul O. Snoke of Lancaster, Pennsylvania, is as anxious as most physicians to retain a close personal relationship with his patients. He feels that one important way to retain this relationship is by enclosing personal notices in monthly statements—a project encouraged by many medical societies.

One of Dr. Snoke's messages contains a warning against travelling from one doctor to another in search of "the magic formula". The note says: "We have a lot of magic drugs but your illness may not be one that will respond to those drugs we know now." Another note asks the patient to realize that the doctor is human and "he gets tired, too . . . . If your doctor is weary, don't scold him for it; perhaps he was up all night with a very difficult case."

Such messages, adapted to the doctor's own personality and to his type of practice, help to wipe out the impersonal label with which some doctors are stamped.

GENERAL PRACTICE

SYMPOSIUM ON CHEST DISEASE

THE FIFTH ANNUAL SYMPOSIUM for general practitioners on tuberculosis and other chronic pulmonary disease will be held at Saranac Lake, New York, from July 9 to 13, 1956. It is approved for 26 hours of formal credit for members of American Academy of General Practice. It is also approved by the College of General Practice of Canada for formal study credits. This course is designed particularly for general practitioners. Many of the sessions are informal panel discussions with ample opportunity for questions from the audience. Sessions will be held in the various sanatoria, hospitals and laboratories in the Saranac Lake area. The faculty will consist of physicians, surgeons and scientists from Saranac Lake as well as guest lecturers. Many doctors attending previous sessions of this symposium have brought their families with them to enjoy the many vacation facilities of the surrounding Adirondack Mountains. So that families may have the use of the family car, free bus transportation will be provided to the various meeting places for the doctors attending the course.

The registration fee for the Symposium is $40. Further information and copies of the programme can be obtained by writing Dr. Edward N. Packard, General Chairman, Symposium for General Practitioners, P.O. Box 262, Saranac Lake, N.Y.

Association Notes

EXECUTIVE COMMITTEE

The Executive Committee of the Canadian Medical Association met in the Board Room of C.M.A. House on March 16, with Dr. Norman Gosse in the chair. The chairman welcomed as newcomers Drs. C. L. Tisdale (Saskatchewan), Arthur Powers (Quebec) and Morley Young (Alberta), and congratulated the President-Elect, Dr. Renaud Lemieux, on his recent promotion in the Faculty of Medicine of Laval University.

It was reported that poor health had compelled Dr. Myron Weaver (Vancouver) to resign from the chairmanship of the C.M.A. Committee on Medical Education; this news was heard with regret, and suggestions were made for a successor, whose appointment will be announced later.

The committee heard with pleasure that Dr. A. J. McGanity (Kitchener, Ontario) had agreed to chair the new Special Committee on Civil Disaster, and had already discussed with Divisions the formation of local disaster services based on hospital staffs.

The Special Committee on Traffic Accidents had much to report. Its nucleus committee had met frequently, and a special meeting of divisional chairmen was due on April 20 and 21. It was hoped also to arrange a further meeting in May to organize a Canadian Foundation for Research in Traffic Accidents, details of which are published on page 557 of this issue. Representatives of the Canadian Medical Association, L'Association des Médecins de Langue Française du Canada, and the Canadian Bar Association would meet with representatives of industry connected with motoring. In planning, close relation with the Cornell Auto Crash Research Unit had been maintained. The Canadian Medical Association would also maintain close relationships with the Foundation. An energetic and dedicated Medical Director would have to be found, and also a statistician and three or four field men to maintain contact with provincial units. Four units (in Quebec, Montreal and Toronto) were ready to go to work on accident problems.

The Treasurer presented a report indicating a satisfactory financial position for the C.M.A. The editor and managing editor also presented their usual reports on the progress of the *Journal*, whose affairs were also in a satisfactory state.

The Committee heard from Dr. R. Lemieux details of the preparations for the 1956 Annual Meeting of the Canadian Medical Association in Quebec. He made the point that the motels of Quebec City were very good, and should not be overlooked by persons seeking accommodation. He also mentioned the Scientific Exhibition. The government of the province of Quebec was contributing an exhibit to this, which should prove extremely attractive. There was still room in the vast building of the Ecole de Commerce for further scientific exhibitors.

It was announced with regret that the physicians of Regina would be unable to sponsor the 1957 Annual Meeting. Edmonton has, however, stepped in, and it is expected that the meeting will take place in the week of June 17-21, 1957, in that city. The Committee also took a look into the future, discussing transportation for the Conjoint B.M.A.-C.M.A. Annual Meeting in Edinburgh, July 20-24, 1959. Travel to this meeting will probably be arranged through the C.M.A. office, side-trips being arranged through an accredited travel agency.

The official opening of the C.M.A. House on the following day was mentioned; an account of this will appear in our next issue.

A proposal was received from the British Columbia Division for the setting up of a com-

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mittee to study and report on the relative responsibilities of the C.M.A. and its Divisions in such subjects as medical economics. It was agreed by the Executive to nominate such a committee.

The Executive Committee heard that the Trans-Canada Medical Plans Commission had approved in principle the proposals to utilize data from the member plans as material for research in prepaid medical care. The roles of C.M.A., T.C.M.P. and member plans in such a research organization were still to be defined, however.

The Executive Committee nominated delegates to the World Medical Association Assembly in Havana, October 9-15, 1956. They agreed that the British Commonwealth Medical Conference should meet in London, England, in 1957, but left the nomination of delegates to a later date. Dr. Routley will represent the C.M.A. at the Annual Meeting of the British Medical Association in Brighton next July, when he will install his successor in the B.M.A. Presidency.

Mr. L. W. Holmes, Assistant Secretary, reported on his public relations activities, which included visits to Divisions. He gave money examples of indications that the medical profession was becoming more interested in public relations, and drew attention to the three recent publications of the Association: (1) the revised Code of Ethics; (2) You and the C.M.A.; (3) Basis of Approval of Hospitals for the Training of Interns in Canada. The Committee was informed that a bilingual member of the public relations staff, Madame Elise Coulombe, had begun work.

It was gratifying to note that liaison with L'Association des Médecins de Langue Française du Canada had been good. Three representatives of L'Association were now participating in the work of the Medical Economics Committee.

Suggestions from the Midwinter Conference of Divisional Secretaries were considered. It was agreed that the provincial secretaries should take the first step in making a survey of medical manpower in Canada, designed to show how existing resources were meeting needs in various areas and in the various branches of medicine. The group insurance schemes for members at present being sponsored by the Ontario and Quebec Divisions were examined by the Committee.

The above are the highlights of a meeting which lasted from early morning to late at night. This compression of an otherwise two-day meeting was necessary to make way for the official opening of C.M.A. House on the following day. The opening was attended by all the members of the Executive Committee, and will be described in our next issue.

PROVINCIAL SECRETARIES' CONFERENCE

CHICAGO in February may not be anybody's idea of a vacation resort, but the warmth of the welcome accorded by the staff of the American Medical Association to our Provincial Secretaries' Midwinter Conference made up for the grimness of the weather, when we met there on February 15 and 16. Why should Canadian secretaries meet in Chicago? There were two reasons for the unusual venue. First there was a long-standing and very pressing invitation from our sister association, conveyed to us by the genial General Secretary, Dr. George Lull, who has been a welcome visitor to our Annual Meetings on many occasions in the past. Secondly, with air travel, Chicago is just as convenient for such a meeting as our major Canadian cities.

In spite of adverse weather conditions, all the secretaries arrived safely to begin two days of informal discussion, punctuated only by a conducted tour of the vast A.M.A. building, in which small groups of visitors were escorted by the charming guides detailed for this task.

Many of the items discussed were, as usual, mainly of secretarial interest. Common problems of organization and management were put to the meeting for solution, and some resolutions were passed for consideration at the next meeting of the Executive Committee of the C.M.A. Membership promotion was mentioned, as well as a number of public relations developments. The new brochure "You and the C.M.A." was examined in detail, and various suggestions were made for its distribution, and for modifications of a second edition. Problems in postgraduate education organization within the various provinces were also described, while medical economics played a big part in the discussions, which naturally centred on questions of health insurance.

On the scientific side, the secretary of the Alberta Division gave an account of the divisional report on operative deaths, with its suggestions for improving anæsthetics training, for limitation of surgery by inadequately trained surgeons, and for increased autopsy work in relation to fatalities at operation. This provoked a discussion of other subjects suitable for study at the divisional level.

The visit to Chicago was not entirely devoted to work. On the first evening of the conference, Dr. George Lull played host to the secretaries at an admirable dinner in gracious surroundings at the University Club. Some of the party were also able to take advantage of the many cultural amenities of the city for a brief period, before the long beat home by plane and train. Our thanks go out to the A.M.A. for their hospitality. We can only hope that we proved as adequate as guests as they did as hosts.

REUNION ANNUELLE: AUX EPOUSES DES CONGRESSISTES

Avec son hospitalité devenue proverbiale, le vieux Québec fera de nouveau un acceuil chaleureux à l'ASSOCIATION CANADIENNE MEDICALE qui y tiendra ses assises en juin procbain.

Les épouses des membres qui assisteront au congrès annuel bénéficieront d'un intéressant programme préparé spécialement à leur intention. Dès la mi-janvier, le comité féminin sous la présidence de Mme. Renaul Lemieux et composé de Mmes. J. de St-Victor, Fr. Letarte, C. A. Gauthier et J. G. Howlett, se réunissait pour établir de façon quasi définitive les cadres des activités féminines. Les sous-comités (inscription, divertissement, fleurs, publicité, réception, transports, emplettes, golf) ont comme présidentes respectives: Mmes. L. P. Roy, Marcel Langlois, Rol. Desmeules, W. H. Delaney, Mat. Samson, J. M. Elliott, Sam. Pollack et Jules Hallé.

Avant de détailler le programme, nous nous devons de souligner le problème, toujours important pour vous Mesdames, de la tenue vestimentaire. Deux réceptions, dont un dîner de gala et un bal, vous obligent à apporter robe longue et habit du soir (full dress) avec cravate blanche pour vos maris. Pour toutes les randonnées par autobus, calèche, bateau, ou même promenade à pied sur notre enchanteresse terrasse Dufferin, il sera prudent d'inclure dans vos bagages costume ou manteau de lainage. Juin est habituellement à Québec un mois splendide, mais la proximité de notre fleuve St-Laurent nous gratifie parfois d'écarts de température assez marqués.

Le *LUNDI, 11 juin,* il y aura inscription à 10 heures a.m. et à 5h p.m. réception par le Gouverneur Général à la Citadelle, sur invitation.

Le MARDI, 12 juin, départ à 10h a.m. pour visite à Ste-Anne-de-Beaupré suivie d'un déjeuner au Manoir St-Castin du Lac Beauport; retour par excursion panoramique des sites pittoresques de la ville de Québec. La journée se terminera par un dîner de gala au Château Frontenac où Son Excellence le Gouverneur Général sera l'invité d'honneur. Une danse suivra avec spectacle de folklore.

Le MERCREDI, 13 juin, journée libre pour les dames jusqu'à 5h p.m. où médecins et leurs épouses se réuniront au Château pour un cocktail, réception donnée par les autorités de la ville.

Ce mercredi, tout comme lundi d'ailleurs, sans programme défini, permettra à celles qui viennent à Québec pour la première fois de visiter les principaux lieux d'intérêt culturel, historique ou religieux de Québec (Musée Provincial, Couvent des Ursulines, Séminaire, Voutes de Talon, Musée de l'université, Ecole des Arts domestiques etc.). Quant à celles qui ne sont pas cette fois des touristes, de nombreuses et ravissantes boutiques d'artisanat et d'antiquités attendent votre visite. Un comité permanent sera d'ailleurs au Château à votre disposition pour tout renseignement concernant magasins, clubs, restaurants, etc. Cette journée se clôturera à 8.30 p.m. par l'assemblée générale annuelle suivie d'un bal qui sera la réception officielle du Président.

Le JEUDI, 14 juin, à 1h p.m. déjeuner au Château avec conférence de M. l'Abbé Maheux. Il y aura à cette occasion tirage de nombreux prix de présence. A 5h p.m. séance académique à l'université Laval suivie d'un vin d'honneur dans les grands salons de l'université, ou, si la température le permet, dans les jardins du Grand Séminaire.

Le VENDREDI, 15 juin, réception d'adieu à 10h a.m. au Château.

ANNUAL MEETING: TO THE LADIES

Quebec, the ancient capital of Canada, and its citizens are looking forward to the C.M.A. Meeting in June and will extend you a warm welcome. If you are interested in the early history of your country (and who isn't?), you will enjoy walking through the old walled city with its quaint narrow streets, visiting Quebec's vast historic storehouse of ancient and modern times, from its founding as a city by Champlain in 1608, to the Empire Conferences with the world's leaders, including Churchill and Roosevelt.

Trips have been planned for you to the surrounding country: Ste. Anne de Beaupré, Montmorency Falls, Lac Beauport, with lunch at the Manoir St. Castin, and a sightseeing tour of Quebec. Time has been allowed for visiting other spots such as the museum, handicraft shops, and the Ursuline Convent.

A shopping counsellor service will be available every day to advise you and answer all your questions. Men may also bring their shopping problems to us. Your Counsellors will be Mrs. S. L. Pollack, Madame J. L. Larochelle and Madame Fernando Hudon.

Madame Renaud Lemieux and her committees have planned an interesting programme for the ladies, which at this moment is subject to some change.

We felt that the ladies may wonder what they should pack. In early June the days are warm but the evenings can be cold. Be sure to have a suit and warm coat on your list. As the Governor-General, the Honourable Vincent Massey, will be guest of honour at the dinner to Council, a full-length evening dress is necessary. The gentlemen must wear white tie, tails and decorations to this dinner, especially those seated at the Head Table. Here is the programme as planned to date:

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Hôpital Laval

MONDAY, June 11:—

10.00 a.m. Registration of Council at the Chateau Frontenac. Hostesses in attendance; coffee will be served.

5.00 p.m. Reception by the Governor-General at the Citadel, upon invitation.

TUESDAY, June 12:—

10.00 a.m. Registration at the Chateau.
Departure, around 10.00 a.m. for Ste. Anne de Beaupré, with lunch at Lac Beauport about 1.00 p.m. Sightseeing tour on the way back.

7.00 p.m. Dinner of the Division, with the Governor-General as guest of honour. Entertainment: folklore. Dancing will follow. *Formal dress* is requested, especially for those sitting at the Head Table.

WEDNESDAY, June 13:—

10.00 a.m. Registration.

5.00 p.m. Civic Reception at the Chateau (Cocktails).

8.30 p.m. Annual General Meeting.
Reception by the President. Ball—*Formal Dress.*

THURSDAY, June 14:—

10.00 a.m. Registration.

1.00 p.m. Lunch at the Chateau with the Abbé Maheux as guest speaker.
Draw for prizes.

5.00 p.m. Academic Session at Laval University followed by a "vin d'honneur" in the reception rooms of the University or, if weather permits, in the gardens of the Grand Séminaire.

FRIDAY, June 15:—

Farewell coffee party at the Chateau Frontenac.

HOPITAL LAVAL

THE CENTRE for the treatment of tuberculosis in Quebec is the Hôpital Laval, which was founded in 1915 as the result mainly of the efforts of Dr. Arthur Rousseau. The original hospital was abandoned in 1918 for a more commodious building (illustrated) on the Heights of Ste. Foy. Since 1946 the Sisters of Charity of Quebec have owned and administered the institution, in which there is now a thriving centre of thoracic surgery with facilities for training and research. The hospital is not far from the Ecole de Commerce where the scientific programme of the C.M.A. will be held next June.

DON'T FORGET THE MOTELS

We hear that everyone going to the Quebec meeting in June wants to be lodged in the tower of the Château Frontenac. Unfortunately, when the tower was built, the builders did not make allowance for this unprecedented rush of Canadian physicians to enjoy the view across the river. But there are other delightful accommodations available in Quebec City. Quite apart from the other excellent hotels, we are assured on good authority that there are motels in Quebec which are second to none. It is even whispered that one of them has the finest dining room in the area. Many doctors will be proceeding to Quebec by motor car, and motel accommodation is made to order. So don't be disappointed if you can't get in the tower. Give the motels a trial instead. Whatever your preference, please complete the housing application form and send it to Dr. Gingras now, while there is still a good choice of accommodation.

HOUSING APPLICATION FORM

89th Annual Meeting, C.M.A. - Quebec, June 11 - 15, 1956

DR. R. GINGRAS,
CHAIRMAN, COMMITTEE ON HOUSING, C.M.A.,
LAVAL MEDICAL SCHOOL,
QUEBEC CITY, QUEBEC.

I am planning to attend the Annual Meeting of the Canadian Medical Association in Quebec City, June 11 to 15, 1956.

Will you please reserve the following:

----------Double room with bath or shower (double bed).

----------Double room with bath or shower (twin beds).

----------Room for----------persons (private bath, or shower).

----------Motel unit for----------persons (bath or shower).

In view of the large attendance expected, the hotels have no single rooms available. It might be to your advantage to share a room with another member. Please mention below the name of the party with whom you would like to share your accommodation, otherwise assignment will be made by the Housing Committee.

Name----------

Names of persons who will occupy the accommodation requested above:

NAMES (Dr. and Mrs.):----------

ADDRESS:----------

I (we) expect to arrive in Quebec on----------June the----------

----------in the afternoon (before 6.00 p.m.) ----------in the evening (after 6.00 p.m.)

Travelling by:---------- Automobile;---------- Train;---------- Air;---------- Bus.

My choice of accommodation is listed below. (Check in order of preference 1, 2 and 3.)

HOTELS:

----------	CHATEAU FRONTENAC	($12.00 to $20.00 for two persons)
----------	CLARENDON HOTEL	($11.00 to $12.00 " ")
----------	HOTEL ST. LOUIS	($8.00 " ")
----------	HOTEL VICTORIA	($10.00 to $12.00 " ")
----------	CHATEAU LAURIER	($8.50 to $10.00 " ")

MOTELS:

----------	AUBERGE DU BOULEVARD LAURIER	($4.00 to $5.00 per person)
----------	MOTEL DU PONT	($4.00 to $5.00 ")
----------	QUEBEC MOTOR COURT	($4.00 to $5.00 ")
----------	L'HABITATION	($5.00 ")
----------	AUBERGE DES 4 CHEMINS	($5.00 to $6.00 ")
----------	MOTEL DES LAURENTIDES	($6.00 ")
----------	MOTEL HELEN'S	($3.00 ")
----------	A B MOTEL	($3.00 ")

TOURIST HOMES:

Near Château Frontenac.
First-class rooms with or without bath ($3.00 to $10.00 per person).

FORMULE DE RESERVATIONS

89ème Réunion annuelle du A.M.C. - Québec, du 11 au 15 juin 1956

DR. R. GINGRAS,
PRÉSIDENT,
COMITÉ DES RÉSERVATIONS, A.M.C.,
UNIVERSITÉ LAVAL DE QUÉBEC,
FACULTÉ DE MÉDECINE,
QUÉBEC, P.Q.

Je me propose d'assister à la 89ème réunion annuelle du A.M.C. qui aura lieu à Québec du 11 au 15 juin 1956.

Prière de bien vouloir faire les réservations suivantes:

----------Chambre avec bain, ou douche (lit double).

----------Chambre pour deux personnes, avec bain ou douche (lits-jumeaux).

----------Chambre pour----------personnes (bain ou douche).

----------Cabines pour----------personnes (bain ou douche).

Vu le nombre imposant d'invités qui participeront à ces assises, les hôteliers nous prient de noter qu'ils ne pourront nous offrir des chambres simples. Sans doute trouverez-vous avantage à partager une chambre avec un confrère. Si tel est votre désir, vous voudrez bien mentionner ci-dessous le nom de la personne avec laquelle vous voulez faire cet arrangement. Si aucun nom n'est indiqué, le Comité de Réservations procedera alors lui-meme à la répartition des chambres.

Nom----------

Noms des personnes occupant les chambres mentionnées ci-haut:

NOMS (Dr et Mme)----------

ADRESSE----------

J'arriverai à Québec----------le---------- juin----------

vers----------h. de l'après-midi (avant 6.00 p.m.) vers----------h. du soir (après 6.00 p.m.)

Moyen de locomotion: Automobile----------Train----------Avion----------Autobus----------

Mon choix d'hôtel est indiqué ci-dessous dans l'ordre de préférence:

HOTELS:

----------	CHATEAU FRONTENAC	($12.00 à $20.00 pour deux personnes)
----------	HOTEL CLARENDON	($11.00 à $12.00 " " ")
----------	HOTEL ST. LOUIS	($ 8.00 " " ")
----------	HOTEL VICTORIA	($10.00 à $12.00 " " ")
----------	CHATEAU LAURIER	($ 8.50 à $10.00 " " ")

MOTELS:

----------	AUBERGE DU BOULEVARD LAURIER	($4.00 à $5.00 par personne)
----------	MOTEL DU PONT	($4.00 à $5.00 ")
----------	QUEBEC MOTOR COURT	($4.00 à $5.00 ")
----------	L'HABITATION	($5.00 ")
----------	AUBERGE DES QUATRE CHEMINS	($5.00 à $6.00 ")
----------	MOTEL DES LAURENTIDES	($6.00 ")
----------	MOTEL HELEN'S	($3.00 ")
----------	A B MOTEL	($3.00 ")

MAISON TOURISTE:

Près du Chateau Frontenac.
Chambre première-classe avec ou sans salle de bain ($3.00 à $10.00 par personne).

MEDICAL MEETINGS

MATERNAL AND CHILD HEALTH CONFERENCE

On January 30 and 31, the first federal-provincial Maternal and Child Health Conference was held in Ottawa under the sponsorship of the Department of National Health and Welfare. The delegates, who were welcomed by the Minister, the Honourable Paul Martin, were provincial health department officials interested in maternal and child health. Seven provinces were represented, including five of the six provinces with divisions of maternal and child health under full-time medical direction.

An interesting analysis of current maternal and infant mortality statistics was presented. It was apparent that Canada had a relatively good record in maternal mortality. In 1954 a maternal mortality rate of 0.7 per 1,000 live births was excelled only by the United States rate of 0.5. However, as is familiar to all health workers, the record in infant mortality was not as good. In 1954 the infant mortality rate was 32 per 1,000 live births, but there were 11 other countries with comparable standards of living with lower rates. That a further reduction of deaths from environmental causes such as pneumonia and gastroenteritis was possible was shown by the fact that Canada's neonatal rate compared more favourably with that of other countries than her total infant mortality rate.

A review of provincial activities revealed that considerable emphasis was now being placed on the extension of programmes for maternal and newborn care.

In general, the participation of provincial health departments in maternal care was limited to the educational field. There was obviously considerable interest in the development of prenatal education programmes, particularly for group instruction of expectant mothers. It was agreed that the understanding and support of the practising physicians in the community was essential to the long-term success of such teaching programmes.

Many provinces were assisting hospitals to improve their care of mothers and newborn, especially prematures. Two steps in this direction were the provision of special equipment for nurseries, such as incubators, and assistance with graduate education of nurses in obstetrics and newborn care. The discussion soon revealed that the availability of training facilities in these fields was a limiting factor which needed further consideration.

The consultant services of the Child and Maternal Health Division of the Department of National Health and Welfare, available to provincial health departments or other health agencies, were outlined. It was pointed out that the Division attempted to serve as a source of information on recommended standards of care for mothers and children and on the organization of health services for them. The preparation of health education materials for both lay and professional use, available through Provincial Health Departments, continued to be a major concern.

A discussion of assistance available for extension of child and maternal health services through the health grant programme centred around the Child and Maternal Health Grant. An analysis of the first two years of its utilization showed that over $190,000 was spent for purchase of technical equipment such as incubators, resuscitators, or croupettes. Funds were also used for the administration of provincial divisions of Maternal and Child Health, for training of physicians and nurses, for services for prenatal care and child health supervision, and for research.

Analysis of the utilization of the Crippled Children Grant showed that during 1954-55 when its utilization had become fairly well stabilized, over 70% of funds were being used for services for poliomyelitis, cerebral palsy, other orthopædic handicaps and cleft palate. Research and other types of assistance such as for orthopædic appliances made up 30%.

Research being assisted under the Public Health Research Grant as well as the Child and Maternal Health Grant and Crippled Children Grant showed a wide range of interest in problems of mothers and children. Among projects receiving assistance were several studies of perinatal mortality, research in the field of isoimmunization and the Rh factor, and studies concerned with maternal health such as a study of abortion and a study of postmaturity. The need for further field research in addition to the clinical and laboratory investigations now under way was emphasized.

It was obvious throughout the two-day meeting that there were many areas of common interest shared among provincial and federal workers in maternal and child health.

At the close of the Conference, appreciation was expressed to the Department of National Health and Welfare for providing the opportunity to exchange ideas and experience in the planning of better health services for mothers and children.

JEAN F. WEBB, M.D., D.P.H.,
Chief, Child and Maternal Health Division.

THE FIFTH PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

The Fifth Pan-American Congress of Ophthalmology was held in Santiago, Chile, from January 8 to 14, 1956, and was attended by ophthalmologists from 17 countries of North, Central and South America.

The President of the Association was Dr. Moacyr E. Alvaro of Sao Paulo, Brazil; the Secretary-General, Dr. Rene Contardo of Santiago. Dr. Henri Pichette of Quebec was a vice-president for Canada, and Dr. A. J. Elliot, of Toronto, an assistant secretary-treasurer. Dr. Mark R. Marshall of Edmonton represented Canada at the Congress.

The intensive scientific sessions were well attended and featured official symposia on 11 subjects: collagen diseases; primary glaucoma; secondary glaucoma; congenital glaucoma; detachment of the retina; psychosomatic ophthalmology; tropical diseases; physiopathology and surgery of the lens; plastic surgery; visual fields and neuro-ophthalmology; intraocular tumours. Rounding out the programme were 40 individual papers, 29 films, and several scientific exhibits of high calibre. A remarkably effective and successful system of simultaneous translation removed most language difficulties. The numerous symposia provided an effective review of recent advances in ophthalmology.

Ocular manifestations are prominent in the diffuse collagen diseases. Although the steroid derivatives can induce temporary clinical remissions, there is as yet no definitive therapy that will prevent or affect the course of most of these conditions.

The outlook for patients with glaucoma has improved, with recent advances in the diagnosis and treatment of this disease. The introduction of tonography, and a better understanding of the clinical applications of provocative tests, diurnal pressure changes and gonioscopy, are permitting earlier diagnoses. Experience is showing the disease to be more amenable to treatment when this is begun early. Diamox has proved to be an important addition to our medical armamentarium. In surgical treatment, peripheral iridectomy, iridencleisis, and cyclodiathermy have become popular, and their indications more clearly defined. These are proving to be safe and conservative procedures, and the operative risk in glaucoma is becoming less. Mass glaucoma-detection studies have shown the incidence of undetected primary glaucoma in the general population to be in the region of 2% for people over the age of 50. General physicians and ophthalmologists should work out a practical and effective means of uncovering these early, symptom-free

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cases, especially since non-medical refractionists are unable to diagnose the disease in its early stages.

The treatment of congenital glaucoma remains less than satisfactory and the over-all prognosis continues poor. However, the operation of goniotomy as described by Barkan, and that of goniopuncture as described by Scheie, have given good results in many cases, and are considered by many to be the operations of choice. Cyclodiathermy also has its advocates.

The surgical treatment of detachment of the retina is passing through a period of change which may be described as revolutionary. Many new and different techniques, and many modifications of these techniques, are being advocated. The principle of approximating retina and choroid and of surrounding the retinal tear with chorioretinal adhesions (by means of diathermy applications to the sclera) remains a fundamental one. But there is a revival of interest in improving the approximation of retina to choroid, on the one hand by various types of scleral shortening procedure and on the other by intravitreal injections (vitreous implants, air injections). Furthermore, these techniques are being used more and more as primary procedures, rather than as last-resort operations. Principles of pre- and post-operative management are also undergoing radical change. It is exciting to watch this new chapter in ophthalmology unfolding so rapidly, with such benefits to the patient. But the average ophthalmologist looks forward with some impatience to the time when those specializing in this phase of our work can reach a greater unanimity of opinion concerning the merits and indications of the many new techniques being advocated.

Psychosomatic disturbances in ophthalmology can be divided into two categories: the hysterical conversion symptoms and neurovegetative dysfunctions. Examples of the former are blepharospasm, asthenopia and photophobia; while examples of the latter are glaucoma, migraine, and central angiospastic retinopathy.

The use of radioactive phosphorus has proven itself a valuable aid in the diagnosis of malignant lesions affecting the anterior part of the eyeball. Technical difficulties still prevent the application of this method to lesions located behind the globe's equator.

In the treatment of the second eye in cases of bilateral retinoblastoma (one eye enucleated), the use of the radiomimetic drug, triethylene melamine (TEM), as a supplement to x-ray, is giving results superior to those obtained by x-ray alone, according to Reese. The addition of TEM allows a cancericidal effect with a lower dosage of x-ray, thus reducing the complications of x-ray therapy, of which the most serious have been late vitreous hæmorrhages.

When a diagnosis of retinoblastoma is made, a thorough search of the second fundus should be made under general anæsthesia. Experience has shown that the lesion in the second eye, when present, is often small, and is being missed in more than half of the cases.

In the hands of most ophthalmic surgeons, the Ridley operation for cataract, in which a plastic implant is inserted *behind* the iris after removal of the lens, has not lived up to expectations because of postoperative complications. Salleras (Buenos Aires) has obtained superior results using Strampelli's method in which a plastic implant is placed *in front* of the iris in the anterior chamber. In four cases, using this method, he obtained a good functional result with no serious complications other than a moderate iritis.

Among many excellent scientific exhibits, that of Dr. G. Fonda on methods of correcting low vision was of particular interest. The use of strong plus lenses, microscopic bifocals and doublet magnifiers produces magnification by making it possible to read at distances close to the eye. A new magnification reading bifocal, manufactured by the American Optical Company, was on exhibit. This is a one-piece bifocal with a 25 mm. circular spot ground in the centre of the outer surface of the lens. The surrounding lens is plano or contains the distance correction. At the present time, the reading additions in production are plus 16.00, plus 24.00, and plus 32.00 diopters. The ability to look up with such strong reading lenses is very advantageous.

At a special session of the Chilean Ophthalmological Society, the Harry Gradle lecture was given by Dr. Frederick Cordes of San Francisco (read in his absence by Dr. Derrick Vail of Chicago) and dealt with graduate training in ophthalmology. Dr. Cordes feels that one year of general rotating internship is sufficient. Following this, a three-year period of graduate training in ophthalmology is a minimum. Any additional time spent in training should come *after* completion of the residency and should be in fields related to ophthalmology.

A guest speaker on the same programme was Dr. Frank Lavery of Dublin, Ireland, who gave his views on the value of orthoptics. He felt that as a diagnostic aid, it was helpful only in the older age group, when the optimum time for surgery had already passed. In measuring the degree of strabismus the cover test is more accurate than the amblyoscope because with the latter there is a stimulus to convergence. The role of orthoptics as an adjunct in the treatment of muscle anomalies is admittedly difficult to evaluate, but he felt it was of little or no value (with the exception of the treatment of amblyopia). Improvement of binocular skills on the amblyoscope does not imply improvement of binocular vision under normal conditions of sight. When questioned, most of his colleagues who prescribed orthoptics admitted that they believe it to be of doubtful value, but prescribed it "because the orthoptist takes a load off the doctor's back", or "because the parents seem to like it". He questioned whether the apparent limitation of its usefulness to occlusion therapy justified the continued training of well-educated girls as orthoptic technicians. In the treatment of amblyopia, greater attention should be paid to the psychological effects on the child of having to wear a patch over one eye. In some children, it was preferable for psychological reasons to be satisfied, at least at first, with the use of atropine drops, combined with the use of a minus 3.00 sph. in front of the atropinized eye.

Other guest speakers were Count Arruga of Spain, who spoke on detachment of the retina, and Dr. Velter of Paris who spoke on congenital glaucoma.

The important role played by a nation's income tax laws in determining the extent of participation in important international medical congresses of this kind was apparent. Only three Canadian ophthalmologists were present, as compared with 114 from the United States. If Canada is to remain in the forefront of world medicine, and the Canadian people to continue to receive a high quality of medical care, it is essential that our income tax laws, as they apply to doctors attending medical conventions, be revised so as to encourage a larger attendance of Canadian physicians at future meetings.

The next Pan-American Congress of Ophthalmology will be held in Caracas, Venezuela, in 1960. The new President is Dr. Brittain F. Payne of New York.

JOHN C. LOCKE, M.D.

THE MONTREAL PHYSIOLOGICAL SOCIETY

The fourth regular meeting of the Society for this season was held in the amphitheatre of the Montreal General Hospital on Monday, February 13. The scientific programme, which started at 8.30 p.m., was preceded by an hour of "open house" of the biochemistry and cardiorespiratory laboratories. Abstracts of the three presentations on the scientific programme follow.

1. **The Value of Hypothermia in the Experimental Production of a Bloodless Field for Abdominal Surgery**; Dr. Fraser N. Gurd, Department of Surgery, Montreal General Hospital and Department of Experimental Surgery, McGill University.

Normothermic animals poorly tolerate occlusion of the aorta above the cœliac axis, or of the inflow channels to the liver. Experimental evidence was presented to indicate that the safe time of such great vessel occlusion is substantially increased under the influence of hypothermia. The possibility of creating a bloodless abdominal field for surgical purposes is suggested by these results. An outline was given of the development of hypothermia as an addition to the clinical armamentarium, together with some salient features of the alterations in physiology associated with this state.

2. **Pulmonary Function Studies in Left Ventricular Failure;** Dr. D. J. McIntosh, Cardio-Respiratory Laboratory, Montreal General Hospital.

Lung volume determinations, using closed circuit spirometry and the open circuit nitrogen rinse-out technique for residual air, were carried out in 25 patients suffering from left ventricular failure. Total lung volumes were found to be low as compared with the predicted normal values, while residual volumes were found to be moderately elevated. The changes are attributed to loss of distensibility of the lungs as a result of pulmonary congestion. The elevated residual volume cannot be accounted for entirely by the lowered expiratory reserve volume and is considered to be due to decrease of lung compliance and possibly a degree of bronchospasm in some instances. Maximum breathing capacities were measured in 15 of the above cases. Values were invariably low, ranging from 29 to 69% of predicted normal figures. The air velocity index was less than unity in 10 of the 15 patients, suggesting that some bronchial obstruction may be present.

3. **Serum Vitamin B_{12} Levels in Patients with Anæmia;** Drs. D. G. Cameron, T. A. Brown and A. English, McGill University Clinic and Department of Hæmatology, Montreal General Hospital, and Dr. E. B. Deschenes, Charles E. Frosst and Co.

The vitamin B_{12} concentration of serum was assayed microbiologically, using *Lactobacillus leishmanii* as the test organism. Observations were made on the sera of over 200 individuals. Uniformly, vitamin B_{12} levels in patients with pernicious anæmia in relapse were low. The sera of patients with chronic liver disease and anæmia have yielded normal to high values. A few determinations from patients with anæmia and chronic renal disease have also demonstrated similar values. The usefulness of this microbiological technique in the elucidation of the pathogenesis of anæmia was discussed.

A. H. NEUFELD

MAIMONIDES MEDICAL SOCIETY OF ONTARIO

Dr. Samuel W. Leslie of Toronto has been elected president of the Maimonides Medical Society of Ontario for 1956.

Other officers are: Vice-president, Henry Fenigstein; Treasurer, Jack Goodman; Recording Secretary, Kenneth R. Freeman; Corresponding Secretary, Allan Sharpe.

At the first executive meeting held on February 1, 1956, which was attended by both the outgoing and incoming executives, the various committee chairmen presented their reports and a very active programme has been developed pertaining to medical, social, and economic subjects for this year.

At the March meeting the guest speaker was Professor Murray, of the University of Toronto Department of Architecture, who spoke on "Architecture as Related to Medical Practice".

At the April meeting it is intended to have an outstanding authority speak on "Business Aspects of Medicine".

The May meeting will be a dinner, to be held at the time of the Ontario Medical Association meeting in Toronto, at which it is hoped to have present many of our out-of-town members.

Because of the many changing trends in medical practice which are altering the economics of practice, plans are being considered which should benefit the members in the fields of health and accident insurance, and also pensions and retirement plans.

AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY —DISTRICT NO. 5

The Annual Meeting of District No. 5 of the American Academy of Obstetrics and Gynecology (consisting of Ontario, Ohio, Michigan, Kentucky, and Western New York State) will be held in the King Edward Hotel, Toronto, on Saturday, May 12, 1956. The tentative programme follows.

9.00 a.m. — Scientific Session: Round Table Discussion.
12.00 noon — Luncheon.
1.30 p.m. — Scientific Session: Panel on Maternal Mortality.
6.30 p.m. — Cocktails.
7.30 p.m. — Dinner.

CANADIAN TUBERCULOSIS ASSOCIATION

The 56th Annual Meeting of the Canadian Tuberculosis Association is being held May 15-19, 1956, at the Sheraton-Brock Hotel, Niagara Falls, Ont. General sessions of interest to both professional and lay groups have been planned for Tuesday and Wednesday, May 15 and 16. Sectional meetings for physicians, nurses, rehabilitation officers and personnel of provincial tuberculosis associations will be held Thursday, Friday and Saturday mornings, May 17, 18 and 19. A detailed programme and other information may be obtained from the Canadian Tuberculosis Association, 265 Elgin Street, Ottawa, Ont.

CANADIAN PSYCHIATRIC ASSOCIATION

The Sixth Annual Meeting of the Canadian Psychiatric Association will be held at the Chateau Frontenac, Quebec City, on Friday, June 15, 1956.

The programme will be divided into three parts as follows:

Scientific Meeting: Morning Session: 9.30 a.m.-Noon. Two papers will be delivered by invited speakers followed by discussants. Afternoon Session: 2.00 p.m.-3.00 p.m. One paper will be delivered, followed by discussants.

Business Meeting: The annual Business Meeting will be held at 3.15 p.m.

Reception and Annual Dinner: A reception and the Annual Dinner will be held commencing at 6.30 p.m. Members, wives and guests are invited to attend.

Canad. M. A. J.
April 1, 1956, vol. 74

CORRESPONDENCE

HISTOPLASMOSIS

To the Editor:

I have read with a great deal of interest the case report of "Pulmonary Histoplasmosis accompanied by Erythema Nodosum" by Dr. J. Nuttall-Smith of Kamloops, B.C. I think serious objection must be made to the very scanty proof that is offered to substantiate the claim that the illness suffered by this young patient was, indeed, due to *Histoplasma capsulatum*.

The x-ray appearance of pulmonary histoplasmosis can be extremely variegated and can mimic almost any condition responsible for pulmonary pathology. To use x-ray appearance as an absolute diagnostic criterion of this condition is, I am sure, not accurate. This is well illustrated in the case under consideration as the x-ray report states "shadowing is present in the left upper zone. It is due to a post primary tuberculous complex, affecting the antero-lateral segment of the left upper lobe."

The histoplasmin skin test is similarly an aid but not an absolute diagnostic criterion. It can be compared to the tuberculin skin test, and may well have been positive before the onset of the patient's illness. That this could occur without any clinical evidence of illness previously, and without any residuum in the pulmonary x-ray appearance, has been very well demonstrated by American investigations. There are numerous examples of cases converting from negative to positive histoplasmin skin sensitivity while under survey with absolutely no subjective or objective evidence of illness in the interim. If it was known that this girl's histoplasmin skin test was negative prior to this illness, a much stronger case could be made for *Histoplasma* as the causative agent. In a similar manner repeated histoplasmosis complement-fixation tests might have revealed a changing titre during and following the illness, a fact which would have strongly supported a diagnosis of histoplasmosis. I should like to emphasize that in spite of the above objections I do not wish to give the impression that I think histoplasmosis is not a very definite possibility in an illness of this type. On the contrary I think that it is a very likely possibility, albeit (in my opinion) still unproved in this case.

I have no information available about how common *Histoplasma* skin sensitivity or actual clinical disease due to histoplasma may be in British Columbia. Here in Southern Ontario in and adjacent to St. Thomas, there have been several cases very suggestive of histoplasmosis with pulmonary infiltrates and calcification, positive skin tests and changing titres of the complement-fixation test. So far, it has not been possible to accomplish the final step, i.e. the isolation of *Histoplasma* itself. This is partly due to the fact that by the time one has thought of the possibility of histoplasmosis probably the best chance of finding the organism in sputum, bone marrow, etc., has passed.

I started last November to skin test with histoplasmin as many patients as possible, both those with pulmonary symptoms or x-ray changes and patients with no obvious illness that might be related to histoplasmosis. A preliminary survey of the results so far indicates clearly that about 50% of the people tested have very strong positive reaction to histoplasmin. This, coupled with the cases listed above and the increasing number of bizarre pulmonary lesions found by x-ray, leads me to believe that histoplasmosis (mostly of a benign character) occurs much more frequently in this locality than has ever been suspected. This possibility is further strengthened by the fact that we are in close proximity to Ohio and Michigan, where histoplasmin sensitivity is known to be high. In the U.S.A. several different outbreaks of unusual pulmonary epidemics which had been labelled "virus pneumonitis", "cave sickness", "atypical pneumonia" and a host of other names were subsequently reinvestigated by those interested in histoplasmosis, and many of them were proven conclusively to be due to *Histoplasma capsulatum*.

I feel strongly that many cases we are calling virus pneumonia or pneumonitis may well be due to *Histoplasma*, and if this possibility is kept in mind and the organism searched for its isolation might be accomplished with little difficulty, confirming without a doubt the real cause of such illness as that described.

14 Hincks Street,
St. Thomas, Ont.,
January 20, 1956.

E. L. BROWN, M.D.

INTRAVENOUS MERCUROCHROME

To the Editor:

About 25 years ago Hugh Young of the Brady Institute in Baltimore published many articles regarding the use of certain dyes intravenously in controlling severe infection not only of the genitourinary system but generally.

I was interested in the use of mercurochrome intravenously, and during the past year have seen a patient whom I looked after many years ago, while on the staff of St. Joseph's Hospital in Hamilton as pathologist. This woman was in her early forties and came into the hospital with a typical temperature of septicæmia. There were discharging inguinal glands on both sides. *Staph. aureus hæmolyticus* was isolated from the pus, and in 12 hours there was a profuse growth in broth from blood cultures. Following Young's advice she was given a maximum dose of 7 mg. per kilo body weight of mercurochrome 1% solution intravenously. It might be noted that her physician had given her up as hopeless. Her temperature dropped from 105° F. within a few hours, and she was given another injection of dye the next day. The important fact is that she recovered and as far as I know is well today.

I mention this in view of the fact that hopeless cases of *Staphylococcus aureus* infection have recently been reported as being resistant to antibiotic treatment. Perhaps one might fall back on intravenous mercurochrome treatment in some of these cases.

F. B. BOWMAN, M.D., F.R.C.P.[C.]
Medical Arts Building,
Hamilton, Ont.,
February 20, 1956.

BRITISH NATIONAL HEALTH SERVICE

To the Editor:

Would it not be wiser if we immigrant physicians from Britain were not to advise on the inevitability or desirability of a National Health Service in Canada? The impact of Canadian surroundings on the new arrival from England must surely convince us that here is a different way of life and one which gives the great majority a standard of living, a chance to better themselves and a chance to enjoy satisfying work conditions, such as this generation of Britons has never known in its own country.

It could be said that North America is what it is partly because of an unrestricted policy of "free enterprise" which has allowed the most efficient systems and individuals to rise to the top, unfettered by government interference. In this way, their influence and the products of their labours, together with the enormous incentives available to any man who cares to work and use his initiative, have made this country a less frustrating and happier place to live in than Britain where bureaucracy

and socialism slow down the pace to that of the administrative government clerks, paid by the month however foolishly or wisely, quickly or slowly they work. One evil outcome of the British National Health Service is the large and pitiful weekly correspondence in the *British Medical Journal* in which the various strata of the Health Service attack and criticize each other or bitterly complain about their inadequate financial rewards compared with those allotted to others from the pre-determined annual medical budget. It is surely more pleasant that the majority of letters published in the *Canadian Medical Association Journal* deal with methods of practising the art of medicine more efficiently. The free system here obviates the necessity for self-pitying correspondence.

Perhaps we should be very careful before we criticize, advise, or in any way attempt to make this new country "just like home". If any British practitioner sincerely believes that the National Health Service in Britain is a better system than that at present existing here, why does he not remain within it? None of our Canadian colleagues, who probably feel that it might appear inhospitable, have told pedantic Britons that they could stay at home if they don't like it here. Perhaps it is better that a fellow Briton should say this.

J. G. ARMSTRONG, M.A., B.M., B.Ch., M.R.C.S., L.R.C.P.

Box 307,
Edmonton, Alta.,
February 11, 1956.

To the Editor:

May I, from the sidelines of age, comment upon your discussion of the British National Health Service? Your correspondent Dr. Geggie is apt to oversimplify a complicated question. The status quo of medical practice in Canada is not good enough, as he seems to think. Dr. Etherington on the other hand is apt to think there is only one way to skin a cat! Canada is not the U.K., nor have Canadians and British the same outlook. A National Service must be Canadian, not British.

From the sidelines may I say I can still feel nostalgic for my solo work on the "frontier", my five horses, my twenty-six hour days, my Mist. Gent. Alk. Cum Nux. and the multitude of old ladies (of both sexes) who lived on it! of Dover's and Gregory's Powders and *I still use* Pulv. Glycyr. Co! I still feel these had—perhaps still have—their place.

Yet this is not the day of solo work—at least not in the settled parts of Canada! It's just not good enough for the needs of the people or modern scientific medicine, however devoted the physician may be. Besides, those who can pay make their way to city specialists (who by the way are not always "specialists"!) and the indigents are left.

Driving home one night under the stars after a hard midwifery case my son's grandfather—my preceptor of long ago—remarked humorously, "My no-pay patients are the best I have! I can do all I like for them—God is their paymaster."

This perhaps still is true, but indigents (or too many of them in a practice) do not permit a man to live, to work, to pay drug and transportation bills and raise a family! What else is there in life?

Besides, the practice of medicine is too big a problem for solo work. A team is needed and this team needs hospital facilities to make practice worth while to patient or to physician. Teams so equipped can meet local needs and can relieve the larger centres of all but the most complicated cases. I speak, of course, only of the smaller centres where, after all, most Canadians live and which under our present system in varying degrees lack adequate medical services.

In the interests of these parts and the people who live in them we need a federal-provincial medical service plan. But a British type of service will not suit this country where conditions are so different. Under our present plan of individual voluntary effort we do not reach all the people who need our care. Prompt restoration of these people to usefulness and efficiency could be an asset of very great importance not only to themselves but to Canada. However, this system should be set up by the medical profession—not by the non-medical bureaucrats.

There is great danger in committee rule—there is great danger in sterilizing the profession so that the practitioner becomes a mere cog in a bureaucratic set-up—a mere signpost referring patients here and there to this or that specialist or clinic or authority or hospital.

There are good doctors and less good doctors—they are not all the same and they must be allowed to sink or swim according to their ability to do the one or the other. When a man's usefulness is gone he must drop out, or be made to drop out by circumstances. There is no use pretending he is useful when he is not.

Paper work is increasing. The countless health schemes—Blue Cross, commercial, benevolent, provincial, compensation—should be absorbed by one compulsory central federal-provincial organization, to the great good of all of us. At present it is quite possible for the ordinary G.P. to deal with a dozen or more of such organizations in a week, as far away as Halifax or Vancouver, with attendant paper work, delay and postal charges. One organization would simplify the whole thing.

In fact, to be acceptable in Canada a health scheme must: (1) be compulsory and universal; (2) be fee-for-service only; (3) be contributory; (4) give free choice of medical attendant; (5) leave territory open to any reputable licensed physician, where he must prove his worth or fall behind—just as in other callings.

Have we the wit in Canada to evolve such a scheme? Have we the wit to make it work? Have we—physicians and patients—the honesty, generosity and devotion to make a go of it? I wonder!

H. J. G. GEGGIE, M.D. (McGill, 1911)

Wakefield, Que.,
February 27, 1956.

P.S.—I believe Australia has a workable scheme. Can the *Canadian Medical Association Journal* give us the details of this scheme? Can it be adapted to Canadian conditions?

TULARÆMIA

To the Editor:

Dr. T. A. Harris's case report of tularæmia in Northern Saskatchewan (*Canad. M. A. J.*, 74: 60, 1956) was of special interest to me and should receive particular attention by Saskatchewan doctors.

Tularæmia or "rabbit fever" is a fairly widespread disease, having been reported from European and Asiatic countries, from all parts of the U.S.A. and various parts of Canada. In Saskatchewan, however, no cases have been reported since 1941. At that time two cases were encountered in the area north of Meadow Lake (adjacent to Loon Lake). Two other cases were suspected several years later in the same area, along with one in the Maple Creek district—although these were not definitely established.

In January 1955, I treated a case (in a local farmer-trapper) and followed it up at intervals until it was finally established as tularæmia by agglutination tests (titre 1,600 dils.) on March 15, 1955. The tests were done by the Division of Bacteriology, Department of Public Health, Saskatchewan.

Dr. H. O. Dillenberg, Provincial Medical Bacteriologist, noted that this was the first case of tularæmia recorded by the Department of Public Health since the foregoing in 1941. This raised the problem of the possible prevalence of the disease in the Nipawin area. We felt that

more cases may be found, and the advisability of publishing this isolated case was considered. However, with the appearance of Dr. Harris's report it is evident that the disease may be more widespread than we thought. You will note that Nipawin is situated in Northeastern Saskatchewan—approximately 300 miles due east of Loon Lake (Dr. Harris's locale).

As this is the midst of the trapping season, the disease may flare up again. I bring this to your attention hoping it will evoke comment which will alert Saskatchewan physicians to a disease that is considered rare in this province.

J. E. SINDER, B.Sc., M.Sc., M.D.

Riome Bldg.,
Nipawin, Sask.,
February 24, 1956.

SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

THE GUILLEBAUD REPORT

The National Health Service is given practically a clean bill of health by the Guillebaud Committee. This committee, so-called after its chairman (a Cambridge economics don), was appointed by the Minister of Health in 1953 "to review the present and prospective cost" of the Service and to make recommendations. According to the committee, the Service "is framed broadly on sound lines" and its record of service is "one of real achievement". Nor could the committee find any evidence to support the charges of widespread extravagance which have been brought against the Service with great regularity. As for recommendations for cutting the cost of the Service, either by increasing income or decreasing the cost, the committee is at a complete loss. Indeed, if its advice is followed, there will be a considerable increase in the outgoings of the Service. The basis for the committee's optimistic retrospect is that, whilst in England and Wales the current net cost of the Service has risen by £60 million, this actually represents a decrease from 3¾% to 3¼% when expressed as a proportion of national resources. It is also pointed out that, mainly because of an increase of 2% in the population, the cost of the Service per head has only risen from £8.12s. to £8.15s.

Perhaps the two most important points made by the committee are that the Service is not an insurance scheme, and that the amount spent upon the Service must depend upon the nation's resources. Insurance contributions by users of the Service represent only a small proportion of the gross cost of the Service: e.g., in 1953-54, £36 million out of a gross cost, in England and Wales, of £460 million. Further, the Service is available to all persons in the country, whether or not they make any insurance contributions. In other words, it is for the nation to decide what proportion of its national income it is prepared to spend on the Service.

CLAIM FOR MORE PAY

The British Medical Association has given notice to the Minister of Health that it proposes to submit a claim for increased remuneration for general practitioners and consultants. This, according to the Association, is "not a claim for new money", but merely for the remuneration which the profession was promised at the inception of the National Health Service. The basis for the claim is the increase in the cost of living. At present rates the average net remuneration of a general practitioner before taxation is £2,222, whilst that of a consultant is £3,500. It is claimed that this is wholly inadequate in view of the fact that a married professional man earning £700 a year in 1938 would today require a sum of £2,600 to obtain a comparable standard of living. Whilst the standard of living of the nation as a whole has gone up by 7% since 1938, the professional man is today 15% to 30% worse off than he used to be. This announcement by the B.M.A. has had a mixed reception in the profession. Those who oppose it express the view that the timing is most unfortunate in view of the Prime Minister's plea for restraint in claims for increases in pay. The Royal College of Physicians of Edinburgh, by an overwhelming majority, has passed a resolution that "no claims for a general increase in medical remuneration based upon the 'betterment factor' should be made at the present time".

RADIO AND TV ANONYMITY

In spite of considerable opposition, the council of the British Medical Association has reaffirmed its rule of anonymity: that "practitioners approached to appear in such programmes, whether for 'sound' or 'visual' broadcasting, should insist on anonymity as part of the contract". According to the Association's ethical committee and its chairman, breaches of this rule have resulted in "grave disturbance of the doctor-patient relationship", and it would be "undesirable and dangerous to countenance any relaxation" of the rule. Indeed, "to act otherwise would lower ethical standards, and might well promote self-diagnosis and self-medication". The extent to which this rule of anonymity is enforced is well illustrated by two incidents. In a recent TV programme in which the secretary of the B.M.A. participated, he was merely referred to as "a spokesman of the British Medical Association". The council of the Association has solemnly passed a resolution to the effect that, when broadcasting or televising, Dr. Harvey Flack, the editor of *Family Doctor*, the Association's flourishing health journal for the layman, cannot even be referred to as "editor of *Family Doctor*". He is only to be referred to as "the editor of a popular medical magazine".

A NEW JOURNAL

The new year has seen the birth of a new medical journal in Scotland—the *Scottish Medical Journal*. This is the sequel to the widely regretted death of the *Edinburgh Medical Journal*. When it became apparent that the latter journal was reaching the end of its tether, negotiations were instituted between the Edinburgh Medico-Chirurgical Society and the Royal Medico-Chirurgical Society of Glasgow. It is as a result of these negotiations that the new journal has come to life, incorporating the *Edinburgh Medical Journal* and the *Glasgow Medical Journal*. The new journal is to be published monthly. In the first issue the editors express the hope that "a medical worker in Scotland with an original article for publication will consider first the claims of the *Scottish Medical Journal*."

THE NEW POLIOMYELITIS VACCINE

Presumably to compensate for what the *British Medical Journal* described as the Minister of Health's "bungling repression of facts about the vaccine", the Ministry of Health has now issued what it designates as "an aide-memoire" about the new poliomyelitis vaccine. Two vaccines are available, both of the Salk type. In one the strains are: Type I Enders modification of Brunhilde; Type II M.E.F. 1; Type III Saukett. In the other vaccine the strains are: Type I Enders modification of Brunhilde; Type II attenuated Y-SK; Type III attenuated Leon. Final formal approval has not yet been given in respect of Types II and III used in the second vaccine.

London, March 1956. WILLIAM A. R. THOMSON

ABSTRACTS *from current literature*

MEDICINE

Primary Aldosteronism, A New Clinical Entity.

J. W. CONN AND L. H. LOUIS: *Ann. Int. Med.*, 44: 1, 1956.

Aldosterone, the newly discovered normal adrenal secretory product, has attracted the attention of a great many clinical investigators because of its apparent role in the pathogenesis of a number of clinical disorders. This extremely potent sodium-retaining corticoid has been found in excessive amounts in the urine of œdematous nephrotics, cardiacs with congestive failure, patients with decompensated hepatic cirrhosis and women with eclampsia.

The syndrome of primary aldosteronism is now firmly established. It is likely that the condition called "potassium-losing nephritis" is a manifestation of primary aldosteronism. A case recently described in England as potassium-losing nephritis is now recognized as one of primary aldosteronism, a large amount of sodium-retaining corticoid having been found in the urine.

The major clinical manifestations of this syndrome are periodic severe muscular weakness, intermittent tetany and paræsthesiæ, polyuria and polydipsia and hypertension. There is no œdema. The characteristic biochemical alteration in the blood is hypokalæmia, hypernatræmia and alkalosis (elevation of pH and CO_2 combining power). Total serum calcium is normal.

Hyposthenuria unresponsive to pitressin, persistently alkaline urine, and mild proteinuria are observed. 17-Hydroxycorticoid and 17-ketosteroid values are consistently normal.

Despite the periodic occurrence of severe muscular weakness, one is impressed with the relative lack of important symptoms at extremely low levels of serum potassium. Another striking manifestation of this syndrome is the great resistance which it offers against attempts at potassium repletion. With very large amounts of supplementary potassium, serum potassium rises but only mildly.

Patients with such clinical and laboratory manifestations should be subjected to adrenal surgery. To date, in all 12 cases of which the writers are personally aware an adrenal cortical adenoma has been found at operation or at autopsy; 9 were cured of primary aldosteronism by surgical removal of the adenoma and the other 3 were recognized in retrospect at autopsy. It is believed, however, that in some patients with this syndrome an adenoma will not be found at operation. Under these circumstances a total or extensive subtotal adrenalectomy (pending future experience) should be performed. The case reported by Wyngaarden *et al.*, typical of primary aldosteronism, had no adenoma at autopsy. One case is said to have been cured by bilateral adrenalectomy.

This study raises a number of questions that demand intensive investigation. Without attempting to speculate upon them, the writers list them as follows:

What is the stimulus for secretion of aldosterone? It is clear from the data that large amounts of aldosterone produced by a tumour for a long period of time failed to depress endogenous production of conventional ACTH. Yet it did suppress something which affects adrenal size, since a significant degree of atrophy was found in the zona fasciculata of the contralateral gland.

What are the physiological functions of aldosterone in addition to its capacity to produce a positive external balance for sodium and a negative one for potassium?

By what mechanisms do large doses of ACTH or hydrocortisone produce diuresis of sodium in either primary or secondary aldosteronism?

What is the relationship of hyperaldosteronism to hypertension?

What is the relationship of hyperaldosteronism to the production of renal arteriosclerosis?

Is aldosterone involved in the production of the so-called "diseases of adaptation"? Nature has now provided for study a condition in man which manifests not only chronic and excessive production of the naturally occurring mineralocorticoid but also biochemical evidence of an intense mineralocorticoid effect in the body. It would be difficult to conceive of a more profound, hormonally produced disturbance of sodium and potassium metabolism. There is obvious "imbalance" between mineralocorticoid and glucocorticoid activity, since the latter has been shown to be quite normal. The condition is associated with hypertension and renal arteriolosclerosis, the former disappearing as the electrolyte disturbance is corrected by removal of excessive amounts of aldosterone.

If the effects in man of chronic, excessive and "unbalanced" mineralocorticoid activity are sought (and this is postulated as the predominant factor in the evolution of "diseases of adaptation"), primary aldosteronism is likely present. S. J. SHANE

Constitutional Hyperbilirubinemia.

M. P. EANET AND I. B. BRICK: *New Eng. J. Med.*, 253: 1062, 1955.

Constitutional hyperbilirubinæmia is frequently unrecognized and misdiagnosed as hepatitis or other serious liver disease. It usually presents as a mild acholuric jaundice. Most cases occur in young adults who may have no symptoms but frequently complain of abdominal pain, easy fatiguability, anorexia and irritability. The only significant physical finding is icterus. There is no enlargement of the liver or spleen. Laboratory findings are negative apart from elevation of the serum bilirubin level, mainly the indirect fraction; there is no bile in the urine.

These patients are usually diagnosed as cases of serious liver disease and subjected to intensive investigation and prolonged treatment with the inevitable development of serious psychological disability. It is essential that the disease be correctly diagnosed; these patients should live a normal life with a normal life expectancy. The disease is often familial but sporadic cases occur.

A detailed case history of a patient with constitutional hyperbilirubinæmia is reported by the authors, who experimented with the effect of steroids (ACTH and cortisone) upon the jaundice. No change occurred in the level of the serum bilirubin; this is of interest since steroid therapy does diminish the serum bilirubin in some cases of jaundice due to hepatic disease and bile duct obstruction. NORMAN S. SKINNER

Induction of Bronchial Cancer by Local Massing of Carcinogen Concentrate in Outdrifting Mucus.

C. C. MACKLIN: *J. Thoracic Surg.*, 31: 238, 1956.

The combined inner surface of the trachea, bronchi and lungs may be imaginatively viewed as an isosceles triangle whose basal part represents the alveoli. Air-borne carcinogens alighting in this catchment basin are moved outward in a progressively narrowing mucus sheet and so become concentrated, particularly in the great bronchi of the hilus, where the surface is only about 1/10,000 that of the total alveolar lining. Here the current is probably slowed on account of diminution in motivating ciliary area and tortuosity of course. The hilar region is thus the seat of specially strong and prolonged cancerizing action, as is indicated by its greater proneness to bronchial cancer. Chronic irritants set up well-known anaplastic changes, crippling and abolishing the cilia and so further retarding the mucus flow, to intensify the action of the contained carcinogens on the underlying epithelium. Inhaled cigarette smoke and smog of cities are regarded as important common carriers of cancer inducers; a special medium is the fall-out from thermonuclear explosions and the radioactive dust of certain mines. The lesser involvement of the trachea in cancer is perhaps explainable by assuming a prior depletion in carcinogens in the mucus which flows along it, and a better elimination mechanism. AUTHOR

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The Effect of Isoniazid on Lipids of the Tubercle Bacillus.

H. P. RUSSE AND W. R. BARKLAY: *Am. Rev. Tuberc.*, 72: 713, 1955.

Tubercle bacilli isolated from the animal host or grown on synthetic media are acid-fast, and it has been suggested that this quality is due in some way to the lipid composition of the organisms. Recent investigations by these authors, previously reported, have shown that tubercle bacilli lose their acid-fastness when exposed to isoniazid. This loss of acid-fastness may reflect an altered metabolism which leads to a change in the normal lipid composition of the tubercle bacillus. To investigate this problem, the lipid composition of tubercle bacilli exposed to isoniazid was compared with the lipid composition of untreated organisms.

It was concluded that one effect of isoniazid on the tubercle bacillus is the quantitative reduction of substances soluble in organic solvents, particularly methanol. The chemical nature of these lipid extracts is yet to be studied, but it is possible that the loss of acid-fastness is associated with this reduction of lipids in isoniazid-treated bacilli.

Exposure of growing virulent tubercle bacilli to high concentrations of isoniazid alters the ability of these organisms to confer tuberculin hypersensitivity on guinea pigs.

These experimental results, in conjunction with previously reported effects of isoniazid on the loss of acid-fastness of the tubercle bacillus, suggest that isoniazid forces growing tubercle bacilli into an altered metabolic pathway incompatible with the physiological life of the organism. S. J. SHANE

SURGERY

A Re-Examination of Certain Aspects of the Histogenesis of the Healing of Cutaneous Wounds.

T. GILLMAN *et al.*: *Brit. J. Surg.*, 43: 141, 1955.

Experimental wounds of animals and human volunteers were biopsied at various stages of healing; views different from those currently accepted are expressed. Incised wounds show epithelium bridging the gap first, before connective tissue. No matter how the wound is sutured, the epithelium inverts into the incision. After three to five days epithelialization is complete and hyperplastic, and connective tissue then reacts from the subepithelial tissue and grows upward. In the 13-15 day period new vessels are seen growing parallel to and not across the incision. Excessive epithelial hyperplasia is also seen along suture puncture wounds. Increase in collagen and diminution in blood vessels are complete at the 15th to 20th day. Elastic fibres are not deposited for several years.

Similar differences were observed during studies of excised wounds, as in burns and donor sites of split grafts. Rapid and early epithelial growth is the first tissue to cover the raw surface, beneath the surface bloodclot. Connective tissue regeneration occurs from blood cells migrating from the blood stream and from perivascular round cells. True granulation tissue is not formed in these uninfected wounds. It is suggested that regenerating epithelium evokes and modifies connective tissue and vascular responses, and that later connective tissue inhibits epithelial overgrowth.

These findings may have medico-legal implications in determining the age of wounds and suggest methods for the investigation of carcinogenesis. BURNS PLEWES

Adenoma of Brunner's Gland.

F. MOFFAT AND W. ANDERSON: *Brit. J. Surg.*, 43: 106, 1955.

A rare case of a large benign tumour of the second part of the duodenum, the source of hæmatemesis and anæmia, is reported from the Toronto General Hospital. The tumour was successfully removed from a 76-year-old woman. BURNS PLEWES

Aspiration of Breast Cysts as a Diagnostic and Therapeutic Measure.

G. P. ROSEMOND *et al.*: *A. M. A. Arch. Surg.*, 71: 223, 1955.

Though many surgeons do not approve of aspiration as a method of diagnosis or treatment of cysts of the breast, the practice is defended, provided the case is re-examined and followed up carefully. In 150 cases, two were carcinomatous and quickly refilled after aspiration. A great advantage is the psychic relief to the patient to be rid of the lump so promptly. Aspiration biopsy is used only in inoperable advanced carcinoma, preceding x-ray or hormone therapy.

The cyst should be aspirated by a surgeon and excision biopsy is mandatory if the fluid is bloody, the mass does not disappear or the mass recurs promptly. Self-examination and careful follow-up are essential.

BURNS PLEWES

Treatment of Mass Civilian Burn Casualties.

W. G. SCHENK, JR., *et al.*: *A. M. A. Arch. Surg.*, 71: 196, 1955.

The triage and treatment of 20 burn casualties, admitted simultaneously following a Cleveland school fire, are outlined. Emphasis is placed on the importance of immediate screening, so that the more severe cases can get the necessary attention. Although desirable in minor fires like this, it is of paramount importance in any large-scale civilian disaster. Those less severely burned who may be transported to a more remote hospital, or who do not require admission, must not tax the facilities available in the immediate vicinity of the fire.

Use of serum albumin and plasma volume expanders is advised rather than use of too much whole blood. The usefulness of polyethylene catheter for cut-downs, especially in mass casualties, is referred to. Veins may be kept patent for longer periods if 5 mg. of heparin is used in each litre of solution. The early employment of tracheotomy as a prophylactic measure rather than as a last minute emergency procedure is stressed.

ALLAN M. DAVIDSON

Phrenic Nerve Traction for Persistent Hiccup (Singultus).

R. E. SLEMMER: *A. M. A. Arch. Surg.*, 71: 927, 1955.

A method of treating persistent hiccup not controlled by the usual means is described. Using local anæsthesia, the phrenic nerve is exposed on the surface of the scalenus anticus, a loop of wire placed around it and brought out through the skin. Traction on the loop is applied to control each paroxysm thereafter. One side of the loop is cut to remove the wire. Fluoroscopy is used to decide which phrenic nerve to expose. BURNS PLEWES

Traumatic Diaphragmatic Hernia.

C. F. SCHNEIDER: *Am. J. Surg.*, 90: 986, 1955.

As a result of the increasing frequency of automobile and other accidents, traumatic diaphragmatic hernia is occurring much more frequently. The doctor treating these cases must always bear in mind the possibility of such injury because initial thorough examination may fail to reveal any physical findings suggestive of such sequelæ to trauma. If the abdominal contents had not herniated through at the time of the accident, they might later as a result of sudden increased intra-abdominal pressure, e.g. in coughing or during anæsthesia for concomitant injuries. Sometimes the initial rent might have been temporarily sealed off with omentum or possibly the attenuated diaphragmatic fibres were sufficiently strong to maintain the diaphragmatic arch intact until a subsequent period of straining.

The left side of the diaphragm is much more commonly involved because of the protective action of the liver on the right. Unlike the congenital and acquired non-traumatic types, those following injury may occur

in any location, not uncommonly tearing the muscle fibres from œsophageal hiatus to anterior costal margin.

Sudden respiratory symptoms or possibly those of intestinal obstruction, with collaborative objective clinical and x-ray evidence of displaced viscera, would reveal the diagnosis. Time, however, must not be wasted in restoring the normal cardio-pulmonary physiology and releasing the strangulating mechanisms. A transthoracic incision, which can be extended into the abdomen if necessary, is advocated. ALLAN M. DAVIDSON

OBSTETRICS

Rupture and Perforation of the Uterus in Association with Pregnancy, Labor and the Puerperium.

K. FEENEY AND A. BARRY: *Brit. M. J.*, 1: 65, 1956.

Forty-five cases of rupture and perforation of the uterus in association with pregnancy are described. There were seven maternal deaths, a mortality rate of 15.5%; six of these deaths might have been avoided. Of 46 fetuses in the 45 cases 20 survived, 22 died and there were 3 abortions and 1 miscarriage.

All women bearing scars of previous uterine operations should receive special care in pregnancy and in labour, if the latter is permitted. The authors do not subscribe to the belief "once a Cæsarean, always a Cæsarean". When vaginal delivery after previous section is contemplated, strict precautions should be adopted. Two cases of combined rupture of the uterus and bladder are summarized. Rupture may develop quickly in neglected shoulder presentation.

Internal version should not be attempted unless the conditions for its safe performance are present. A bad failure of forceps delivery may cause serious trauma. Abortions should be cleared out under direct vision. The soft subinvoluted puerperal uterus is easily perforated.

Hydrocephalus is a potentially dangerous complication because minor and moderate degrees are easily missed. Diagnosis, both clinical and radiological, is not as easy as the textbooks indicate.

Before delivery, posterior pituitary extract should be used with great care.

High multiparity provides problems, one of which is the possibility of spontaneous rupture of the uterus. The causes of dystocia in the multipara are summarized. Brow presentation should always be considered when the fetal head fails to descend in the second stage of labour, especially in the multipara. Precipitate labour may cause serious trauma to the mother and fetus.

Women who have had plastic cervical and vaginal operations should be delivered in hospital.

Spontaneous rupture of the vaginal and supravaginal cervix with extension into the broad ligament is described. Four clinical varieties of rupture are described. The "quiet" and "delayed" varieties are easily missed. Stress is laid on early diagnosis. Treatment is summarized. The value of transfusion is stressed.

The incidence of rupture and perforation of the uterus in association with pregnancy was 1 in 1,200 of all deliveries in the service of Coombe Lying-in and National Maternity Hospital, Dublin. ROSS MITCHELL

Pregnancy After Forty-four.

E. F. STANTON: *Am. J. Obst. & Gynec.*, 71: 270, 1956.

The rate of abortion after 44 years of age is very high, approximately 33%. After 47 years of age abortion occurs in about 80% of pregnancies. Spontaneous delivery in this older age group occurs with an incidence comparable to the over-all rate. Cæsarean section is employed with over twice the usual frequency.

Prolongation of labour over 30 hours is about 10 times as frequent in these cases. Toxæmia is three times as common as the over-all annual incidence, and severe pre-eclampsia occurs nine times as often as in the total pregnancies for the year. The incidence of hydatid mole is over 20 times that usually encountered on the combined obstetrical and gynæcological services.

Infants of excessive size are twice as common as usual. The incidence of pregnancy occurring 10 or more years after the birth of the last child is 35%. The stillbirth and neonatal death rate will be about nine times the over-all annual incidence. The occurrence of mongolism and congenital malformations incompatible with life is about 4% or approximately eight times the over-all annual incidence. The incidence of viable births after 47 years of age is 1 in 11,000 deliveries.

Pregnancy after 50 years of age is exceedingly rare. A viable birth at 50 years or over practically never occurs. Pregnancy after the menopause is very uncommon, and a viable birth after the menopause is almost unknown. ROSS MITCHELL

Pelvic Endometriosis.

H. ULFELDER: *New England J. Med.*, 254: 12, 1956.

Endometriosis was found in 18% of 400 consecutive gynæcological laparotomies but it was the significant lesion in only two-thirds of the cases. Hysterectomy, with excision of all areas of disease (but without castration except for special indications), is a dependable procedure for cure. Symptoms can usually be successfully relieved by excision of all areas of disease without removal of uterus, tubes or ovaries. This policy of "radical conservationism" is advocated by the author, as conception followed in about one-quarter of the cases so treated.

Over half of the patients in whom the clinical diagnosis of endometriosis was made, but in whom surgery could be avoided, subsequently conceived. The sublingual administration of testosterone relieved pain, perhaps enhanced fertility, and caused no undesirable side-effects in these patients. NORMAN S. SKINNER

The Fetus Can Bleed.

B. CHOWN: *Am. J. Obst. & Gynec.*, 70: 1298, 1955.

Three cases are reported, two of nonhæmolytic anæmia of the newborn with recovery, and one of fatal hæmorrhage in an erythroblastotic baby. In the first case the mother lost more blood in the third stage of labour than usual and a gross defect was found in the placenta. It is suggested that the fetus bled into and through its placenta, producing anæmia in itself and a concealed retroplacental hæmorrhage in the mother. In the second case it was proved that the baby had bled symptomlessly into the mother's circulation, and that the bleeding had been going on probably for several weeks before delivery. In the third case the mother had a chill and fever a few hours before delivery; there was a small defect in the placenta; the baby began to bleed a few minutes after birth. It is suggested that the mother's chill and fever were reactions to transfusions of the incompatible blood of the baby, and that the bleeding in the baby in some way resulted from this reaction.

ROSS MITCHELL

DERMATOLOGY

Basal-Cell Epithelioma Perstans.

M. J. SCOTT: *A.M.A. Arch. Dermat. & Syph.*, 72: 409, 1955.

The author presents a case of basal cell carcinoma which first appeared at age 5 and had no perceptible change up to age 26, when it was first seen by a dermatologist. Clinically the lesion was typical of a basal cell carcinoma. Histological examination confirmed this diagnosis. The author gives reports of similar cases in the literature. He uses the term *perstans* to differentiate it from the usual basal cell carcinoma seen in children.

ROBERT JACKSON

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FORTHCOMING MEETINGS

CANADA

ONTARIO MEDICAL ASSOCIATION, Annual Meeting, Royal York Hotel, Toronto. (Executive Secretary, Dr. Glenn Sawyer, O.M.A., 244 St. George Street, Toronto 5, Ont.) May 9-11, 1956.

CANADIAN TUBERCULOSIS ASSOCIATION, 56th Annual Meeting, Sheraton-Brock Hotel, Niagara Falls, Ontario. (C.T.A., 265 Elgin Street, Ottawa, Ont.) May 15-19, 1956.

CANADIAN PUBLIC HEALTH ASSOCIATION, 44th Annual Meeting, Admiral Beatty Hotel, Saint John, New Brunswick. (Dr. G. W. O. Moss, Honorary Secretary, 150 College St., Toronto 5, Ont.) May 29-31, 1956.

CANADIAN SOCIETY OF PLASTIC SURGEONS, Annual Meeting, Chantecler Hotel, St. Adèle, Quebec. (Secretary-Treasurer, Dr. J. A. Drummond, 1414 Drummond Street, Montreal 25, Que.) June 1-2, 1956.

CANADIAN OPHTHALMOLOGICAL SOCIETY, 19th Annual Meeting, Chateau Frontenac, Quebec, Que. (Dr. R. G. C. Kelly, 90 St. Clair Avenue West, Toronto 7, Ont.) June 7-9, 1956.

CANADIAN UROLOGICAL ASSOCIATION, 12th Annual Meeting, Alpine Inn, Ste. Adèle, Quebec. (Dr. D. Swartz, Secretary, C.U.A., 332 Medical Arts Building, Winnipeg 1, Man.) June 7-9, 1956.

SOCIETY OF OBSTETRICIANS AND GYNÆCOLOGISTS OF CANADA—1956 Annual Meeting, Manoir Richelieu, Murray Bay, Quebec. (Dr. F. P. McInnis, Secretary, Society of Obstetricians and Gynæcologists of Canada, 1230 Avenue Road, Toronto, Ont.) June 8-10, 1956.

CANADIAN MEDICAL ASSOCIATION, 89th Annual Meeting, Ecole de Commerce, Quebec, Que. (Dr. A. D. Kelly, General Secretary, Canadian Medical Association, 150 St. George Street, Toronto 5, Ont.) June 11-15, 1956.

UNITED STATES

INTERNATIONAL ANÆSTHESIA RESEARCH SOCIETY CONGRESS, Flamingo Hotel, Miami Beach, Florida. (Dr. T. H. Seldon, Mayo Clinic, Section on Anæsthesiology, Rochester, Minn.) April 9-12, 1956.

AMERICAN COLLEGE OF ALLERGISTS, 12th Annual Meeting, Hotel New Yorker, New York, N.Y. (Dr. F. W. Wittich, 401 LaSalle Building, Minneapolis 2, Minn.) April 18-20, 1956.

INTERNATIONAL ACADEMY OF PATHOLOGY, 45th Annual Meeting, Cincinnati, Ohio. (Central Office, Armed Forces Institute of Pathology, Seventh Street and Independence Avenue S.W., Washington 25, D.C.) April 24-25, 1956.

AMERICAN GASTROENTEROLOGICAL ASSOCIATION, Annual Meeting, Atlantic City, New Jersey. (The Secretary, A.G.A., University Hospital, Ann Arbor, Mich.) April 27-28, 1956.

AMERICAN GOITER ASSOCIATION, Drake Hotel, Chicago, Illinois. (Dr. J. C. McClintock, 149½ Washington Avenue, Albany, N.Y.) May 3-5, 1956.

MOUNT SINAI HOSPITAL OF GREATER MIAMI, Sixth Annual Seminar, Fontainebleau Hotel, Miami Beach, Florida. (Dr. Harold Rand, Chairman, 4300 Alton Road, Miami Beach, Fla.) May 17-20, 1956.

NATIONAL TUBERCULOSIS ASSOCIATION: AMERICAN TRUDEAU SOCIETY, Statler Hotel, New York, N.Y. (N.T.A., 1790 Broadway, New York 19, N.Y.) May 20-24, 1956.

CATHOLIC HOSPITAL ASSOCIATION OF THE U.S. AND CANADA, 41st Annual Convention, Milwaukee, Wisconsin. (C.H.A., 1438 South Grand Boulevard, St. Louis 4, Mo.) May 21-24, 1956.

AMERICAN COLLEGE OF CHEST PHYSICIANS, 22nd Annual Meeting, Hotel Sherman, Chicago, Illinois. (Executive Offices, A.C.C.P., 112 East Chestnut Street, Chicago 11, Ill.) June 6-10, 1956.

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY, 10th Annual Meeting, Claridge Hotel, Atlantic City, New Jersey. (Dr. W. T. Liberson, Secretary, E.E.G., V.A. Hospital, Northampton, Mass.) June 15-17, 1956.

WORLD CONFEDERATION FOR PHYSICAL THERAPY, Second International Congress, New York, N.Y. (Canadian Physiotherapy Association, 8 Bedford Road, Toronto 5, Ont.) June 17-23, 1956.

SECOND INTERNATIONAL CONGRESS ON PHYSIOTHERAPY, New York, N.Y. (Miss M. Elson, American Physical Therapy Association, 1790 Broadway, New York, N.Y.) June 17-23, 1956.

SOCIETY OF NUCLEAR MEDICINE, Hotel Utah, Salt Lake City, Utah. (Secretary, Dr. R. G. Moffat, 2656 Heather Street, Vancouver 9, B.C., Canada.) June 21-23, 1956.

OTHER COUNTRIES

ASSOCIATION OF CLINICAL PATHOLOGISTS, Cheltenham, England. (Dr. W. H. McMenemey, Maida Vale Hospital for Nervous Diseases, London W. 9, England.) April 7-9, 1956.

FIFTH PAN AMERICAN CONGRESS OF OTO-RHINO-LARYNGOLOGY AND BRONCHO-ŒSOPHAGOLOGY, San Juan, Puerto Rico. (Dr. C. E. Munoz MacCormick, Apartado 9111, Santurce 29, Puerto Rico.) April 8-12, 1956.

NATIONAL ASSOCIATION FOR MENTAL HEALTH, Annual Meeting, Harrogate, England. (Miss Applebey, O.B.E., 39 Queen Anne Street, London W.1, England.) April 12-13, 1956.

INTERNATIONAL CONGRESS FOR THE SOCIAL REHABILITATION OF THE LEPER, Rome, Italy. (M. F. Sarsale, International Congress for the Rehabilitation of the Leper, Via Condotti, Palazzo Malta, Rome.) April 16-18, 1956.

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND, Annual Meeting, London, England. (The Secretary, 45 Lincoln's Inn Fields, London W.C.2.) April 19-21, 1956.

ROYAL SOCIETY FOR THE PROMOTION OF HEALTH, Annual Congress, Blackpool, England. (Mr. P. Arthur Wells, R.S.P.H., 90 Buckingham Palace Road, London S. W. 1, England.) April 24-27, 1956.

LATIN SOCIETY OF OPHTHALMOLOGY, Second Congress, Madrid, Spain. (Dr. Costi, Montalban 3, Madrid.) April 24-28, 1956.

BRITISH PÆDIATRIC ASSOCIATION, Annual Meeting, Windermere, England. (Dr. P. R. Evans, Institute for Child Health, Great Ormond Street, London W.C. 1, England.) April 25-27, 1956.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM, Annual Congress, London, England. (The Secretary, O.S.U.K., 45 Lincoln's Inn Fields, London, W.C. 2) April 26-28, 1956.

INTERNATIONAL UNION FOR PUBLIC HEALTH EDUCATION, Third Conference, Rome, Italy. (M. Lucien Viborel, Secretary-General, 92 rue St. Denis, Paris Ier, France.) April 27-May 5, 1956.

NINTH WORLD HEALTH ASSEMBLY, Geneva, Switzerland. (World Health Organization, Palais des Nations, Geneva.) May 9, 1956.

INTERNATIONAL FERTILITY ASSOCIATION, SECOND WORLD CONGRESS, Naples, Italy. (Prof. G. Tesauro, President of Committee Arrangements, S. Andrea delle Dame, 19, Naples.) May 18-26, 1956.

INTERNATIONAL MEDICO-ATHLETIC FEDERATION, 11th Congress, Buergenstock, Switzerland. (Dr. G. Schoenholzer, Secretary-General, Bluemlisalpstr. 7, Muri-Berne, Switzerland.) May 29-June 1, 1956.

OBITUARIES

DR. RICHARD CHARLES ADAMS, 49, consultant in anæsthesiology, died of a heart attack in Rochester, Minnesota, late in January. Dr. Adams was born in Woolner, Ont., and graduated in 1931 from Queen's University. He interned in the Ottawa General Hospital and then went to Rochester as a fellow in anæsthesiology in the Mayo Foundation, where he subsequently held various senior posts.

DR. ALFRED GEORGE ALLEN, general practitioner of Harper, Washington, died late in January at the age of 89. Dr. Allen was born in Kingston, Ont., and graduated from Queen's University. He practised in Deseronto and Gananoque before moving to the United States.

Dr. Allen is survived by his widow and one son.

DR. CHARLES E. ANDERSON, 71, director of communicable diseases in the Alberta Department of Public Health, died in hospital at Edmonton on February 21. A native of Oil Springs, Ont., Dr. Anderson graduated from the University of Toronto in 1910 and in 1911 started general practice in Brooks, Alta. He served overseas in the First World War and rejoined the forces in 1941, holding the post of garrison medical officer in Edmonton until 1944. He was assistant to the pensions examiner for the federal government until 1952 and joined the Alberta department in 1953.

Dr. Anderson is survived by his widow and a daughter.

DR. LAWRENCE BERNARD BRAINE, a well-known medical practitioner who served in several Nova Scotia communities, died suddenly of a heart attack at his home in Glen Margaret on February 9. Dr. Braine, who was 76 years of age, was born in Halifax, and graduated from the Dalhousie University Medical College in 1900. He began his professional career at Glen Margaret, but later moved to Wyoming. During World War I he served with the Royal Army Medical Corps. After his discharge from that service in 1918 he practised at Annapolis for 30 years.

Dr. Braine is survived by his son, the Rev. R. W. Braine of St. John's United Church in Halifax, and three daughters.

DR. THEODORE WILLIAM BROKOVSKI, 39, Winnipeg general practitioner, died on February 19. He was born in Winnipeg, and attended the University of Manitoba. He then went abroad and studied medicine at the University of Wales, Cardiff. After graduation he served with the Sherbrook Fusiliers Tank Regiment. He was wounded in France and received his discharge with the rank of captain in 1945. On his return to Canada he took up practice in Winnipeg.

Dr. Brokovski is survived by his widow and a daughter.

DR. WILLIAM BUCKELL died at his home in Cowichan, Vancouver Island, on January 2 in his 100th year. He was to have been the guest of honour at the spring meeting of the B.C. Surgical Society. Dr. Buckell was born in Romsey, England, and graduated from University College Hospital, London, before the days of antiseptic surgery. He practised in Cheltenham until the age of 60 and then came to Canada to join his brother, Dr. Edward Buckell. Although blind in his later years Dr. Buckell retained a keen interest in medical news and corresponded with many physicians.

Dr. Buckell is survived by his two daughters and a granddaughter.

DR. KEITH GORDON, a surgeon in the outpatient department of Sunnybrook Hospital, Toronto, died suddenly on February 26 at the age of 55. Dr. Gordon, who was born in Caledonia, was a graduate of the University of Toronto and had served during the Second World War with the R.C.A.S.C.

He is survived by his widow, a son and a daughter.

DR. HAROLD IRVINE, 61, a member of the staff at Westminster Hospital, London, Ont., died on February 16 after a brief illness. Dr. Irvine was born in Sarnia and before going to London practised medicine at Brigden for 25 years. He served in the Medical Corps during both World Wars.

He is survived by his widow, two sons and a daughter.

DR. W. J. KAINE, 73, of Brattleboro, Vt., general practitioner and former health officer, died on January 26 after a short illness. A native of Brattleboro, he graduated in medicine from McGill University in 1911. He interned in Montreal and then practised in Megantic, Que., before returning to Brattleboro.

Dr. Kaine is survived by his widow and three sons.

DR. WILLIAM DAVIS KENNEDY, 83, former general practitioner of Vancouver, died in February. Dr. Kennedy was born in Ottawa and graduated from Queen's University in 1908. He set up practice in Vancouver the following year and retired in 1951.

Dr. Kennedy is survived by his widow, a son and a daughter.

DR. GEORGE EDWARD JURBEN LANNIN, 75, a Hamilton, Ont., general practitioner, died on January 20 after a long illness. He was born near South Mountain, Ont., and graduated in medicine from McGill University in 1907. He set up general practice in Hamilton the following year and continued in practice, with two interruptions for postgraduate studies, until his retirement in 1955. In 1914 he spent several months in Vienna pursuing special surgical studies, and in 1927 went to Edinburgh to obtain his fellowship in the Royal College of Surgeons.

Dr. Lannin is survived by his daughter.

DR. ZENON LESAGE, governor of Montreal Jail at Bordeaux and a former member of the city council and the Quebec Legislative Assembly, died suddenly on February 4 at the age of 68. Dr. LeSage was born at Ste. Therese de Blainville, and graduated from Laval University (Montreal). He then went into private practice. He was appointed governor of Montreal Jail in 1944 while serving on the Montreal city council.

Dr. LeSage is survived by his widow and a daughter.

DR. ALEXANDER LAUCHLAN McQUARRIE, 77, B.C. general practitioner for 45 years, died in Vancouver on February 6. Dr. McQuarrie was born in Ottawa, graduated in medicine from St. Louis University, Missouri, in 1909, and set up practice in British Columbia the same year. He served overseas during World War I and received his discharge with the rank of captain. Dr. McQuarrie opened a practice in Vancouver in 1936, and until his retirement in 1953 had also served as medical examiner with the Department of Indian Affairs.

Dr. McQuarrie is survived by his widow, a son and a daughter.

DR. F. P. MOREAU, 73, who spent 34 years as a medical practitioner in Saskatchewan before his retirement in 1946, died on February 6 in Edmonton, Alta. He was born in St. Bernard County, Que., and graduated from Laval University Medical College in 1908. He went to Saskatchewan the same year and practised in Prince Albert and Hoey.

Dr. Moreau is survived by his widow and four daughters.

DR. OMER NOEL, 72, for 21 years superintendent of St. Jean de Dieu Hospital, Montreal, died at the end of January. Dr. Noel graduated from Laval University in 1908 and then joined the staff of the St. Jean de Dieu Hospital. In 1927 and 1928 he studied psychiatry at the Sorbonne in Paris. He was with the Montreal Hospital

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until 1952. He was also a professor at the University of Montreal and for many years was associated with the Montreal Department of Health.

Dr. Noel is survived by his widow and two sons.

LT.-COL. WILLIAM R. SLACK, M.D., aged 46, was killed in an accident in Korea on February 4. An obituary notice appears under *Canadian Armed Services* on page 598.

MAJOR GEORGE LINCOLN STOKER, M.D., died suddenly on January 27 at the age of 44. See *Canadian Armed Services,* page 598.

DR. HENRY ALLAN TURNER, 87, general practitioner of Millbrook, Ont., died on February 9. He was born in Millbrook and graduated from Trinity Medical College, Toronto, in 1890. Dr. Turner then set up practice in Millbrook, where he became the owner of the local telephone service, power plant, and drug-store. He also opened a small hospital above the store.

Dr. Turner is survived by his widow and two daughters.

DR. MONSON J. WARDROPE, 86, Springhill, N.S., practitioner, died on February 19 after a short illness. A graduate of Dalhousie University, he went to Springhill in 1904.

Dr. Wardrope is survived by his widow.

DR. JAMES M. WATERS, 83, former medical missionary with 20 years' service in India, died on February 28. Born at Lobo near London, Ont., he graduated in medicine from Trinity Medical College, Toronto, in 1901. He and his wife went to India in 1903 for the Presbyterian Church. They returned in 1923 when the doctor joined the staff of the Toronto Bible College. He was registrar until his retirement in 1950.

Dr. Waters is survived by his widow and one son.

DR. ANDRE JOSEPH CIPRIANI. The sudden death of Dr. A. J. Cipriani in the Deep River Hospital on February 23, a few hours after a stroke, came as a great shock to his wide circle of friends by whom he will be greatly missed, and has removed the leading authority in Canada on the biological and medical aspects of atomic energy at the age of 47. As Director of the Biology Division of the Atomic Energy of Canada Limited Plant at Chalk River since the start of the Project, he had become a scientist of international reputation in this field of research and created a laboratory that is unique in the breadth of fundamental and applied investigations, which its staff are performing. He pioneered the development of the cobalt-60 beam therapy units which are used for the treatment of cancer. These units of high specific activity were first made at Chalk River and have been supplied to hospitals in Canada, the United States, Europe and elsewhere. His unique background of education, combined with his native ability, popularity and striking personality, all contributed to the success he achieved in advancing a realistic understanding of the many problems associated with the use of radioisotopes, radiation hazards, and the lethal effect of irradiation on living cells.

He was a member of numerous national and international committees where his wide knowledge of the biological and medical field, as well as the basic physics and mathematical principles involved, was eagerly sought and his advice followed. He was Canada's representative on the International Commission on Radiological Protection and was Chairman of that Commission's sub-committee on the handling and disposal of radioistotopes. He was the Canadian representative on the United Nations scientific committee to study the effects of atomic radiation. He assisted in the organization and training of the army radiation detection unit, and as a result of his firm control and administration of the health physics programme, no employee at the Chalk River Plant has received excessive harmful radiation. He contributed many scientific papers to various international meetings, including the Geneva Conference last August, and also to journals, as well as writing sections for British medical encyclopædias. He was a Fellow of the Royal Society of Canada, Section V.

Dr. Cipriani was born in Port of Spain, Trinidad, on April 2, 1908, the son of the late Leo P. Cipriani and Helene Cipriani. He came to McGill University in 1928 with a scholarship, entering the Faculty of Applied Science with the intention of becoming an engineer. But his excellent ability in mathematics and physics led him to change in his third year to the honour course in mathematics and physics, from which he graduated with high first-class standing in 1932, receiving his B.Sc. degree. After a year of demonstrating in the physics department, during which period he completed some further engineering courses, he decided to study medicine and entered that Faculty at McGill. He interrupted his course for two years to assist Dr. Wilder Penfield and his staff with the design and construction of electronic equipment in connection with neurophysiology. He received his M.D. and C.M. degrees in 1940. During the Second World War he served in the Canadian Army as a medical officer doing research on various medical problems, including that of motion sickness. On the conclusion of hostilities he joined the Atomic Energy Project when the construction at Chalk River commenced.

Cipriani was a man of striking personality and on meeting him one was immediately impressed with his ability, his genial interest in people and outdoor life. He was popular among scientists and local country inhabitants alike, well known throughout the Ottawa Valley towns and villages as an enthusiastic fisherman with great ichthyan skill. Many a visitor to the Project has enjoyed a pleasant day fishing under his guidance. He worked hard, and was a man of action with sound judgment which made him such a desirable member of any committee. He was fond of children, and took special pleasure in interesting them in natural phenomena, be it insects of various kinds which he bred at the laboratory, or flowers and geological specimens. Any week-end in the summer, he could be seen in his open Model A Ford car, which he found useful for fishing expeditions, giving his own and other children a ride round the village, managing a huge load of active youngsters with a kindly but firm discipline, which they respected. He was an active member of the Deep River Branch of the Canadian Legion and First President of the Local Chapter.

Dr. Cipriani is survived by his widow, Alice, and four daughters: Janet Helen, aged 10; Mary Louise, 8; Julia Anne, 6; and Katherine Joan, 5, all of Deep River. Other surviving relatives are his mother, his brother Jean, and three sisters, Louise Cipriani, Madelaine Cipriani, and Marie de Pass, all of Port of Spain, Trinidad.

The funeral service was held February 26, in the Roman Catholic Church, "Our Lady of Good Counsel", Deep River, and was attended by a large number of local and out-of-town friends, many of whom accompanied the remains before interment in Pembroke.

DAVID A. KEYS,
Deep River, Ontario.

DR. GEORGE RAY JOHNSON of Calgary died on Monday, February 13. Dr. Johnson was born in a Methodist parsonage in Welsford, Queen's County, New Brunswick, on October 9, 1877. He attended college at Sackville, New Brunswick, and graduated with a B.A. degree in 1898. He then started his medical studies at the College of Physicians and Surgeons of Baltimore, returning to Canada to complete his medical education at McGill. He graduated in 1902.

For two years he went to sea as a ship's doctor along the West Coast of Africa, and in the Far East. For three years after his return to Canada, he was medical officer to survey parties mapping the route of the Canadian Northern Transcontinental Railway through Northern Ontario. In 1908 he entered practice in Banff with the late Dr. R. G. Brett. In 1909 he moved to Calgary. He served overseas from 1915 until 1918, and after discharge was director of the Department of Soldiers' Civil Re-establishment until June of 1928, when he returned to private practice.

From 1922 until 1945 he was Registrar of the College of Physicians and Surgeons of Alberta and Honorary Secretary-Treasurer of the Canadian Medical Association, Alberta Division. As Secretary he played a prominent part in developing the close liaison between the College and the Medical Association. He was also active in establishing the Alberta Medical Association as a division of the Canadian Medical Association in 1935.

Dr. Johnson was a member of the Medical Council of Canada for many years, and in 1946 was its President. In 1952 he was made a senior member of the Canadian Medical Association. Dr. Johnson was coroner in Calgary from 1928, and later became chief coroner for the area.

Recreationally, Dr. Johnson became very much interested in the natural beauty of the rocks of Canada. He built his own workshop, and spent many hours in the polishing of rocks. He was also a collector of stamps and coins, and, as a Westerner by adoption, became a student of Indian lore.

Dr. Johnson is survived by his widow, Alice, of Calgary; a son, G. R. Johnson, Jr., of Toronto; a brother, Dr. H. H. Johnson, of Calgary; and a sister, Lillian B. Johnson of Wolfville, N.S. W.B.-M.

DR. MALCOLM T. MacEACHERN. All those connected with hospital affairs on this continent learned with regret of the death in Chicago on February 3 of Dr. Malcolm T. MacEachern, a great leader in raising standards of medical care in the hospitals of North America.

Dr. MacEachern was born at Argyle, near Lindsay, Ont., on August 27, 1881. Like so many Canadian doctors of that age group, he began his career as a school teacher, and he followed this profession for four years. He then entered McGill Medical School, from which he graduated in 1910. After early work in Montreal, he went to Vancouver General Hospital as General Superintendent in 1913 and stayed until 1922 when he was appointed Director General of the Victorian Order of Nurses for Canada. In 1923 he joined the American College of Surgeons as Associate Director and served the College in that capacity and as Director until 1951, when he finally joined the American Hospital Association as Director of Professional Relations.

Dr. MacEachern's great contribution to the American College of Surgeons and to the hospital world in general was the development of the Hospital Standardization Program, since then transformed into the work of the Joint Commission of Accreditation of Hospitals. Among many other activities, Dr. MacEachern founded the well-known course in hospital administration at Northwestern University, Chicago, in 1943 and remained associated with the programme until his death. Dr. MacEachern's honours were many. His own university, McGill, gave him an honorary doctor of laws degree in 1950, and in 1939 he received the Award of Merit of the American Hospital Association for outstanding contributions to hospital advancement. We extend our sympathy to Mrs. MacEachern and his daughter, Isobel MacEachern Mackie.

DR. ERNEST GORDON TURNBULL of Barrie, Ontario, who was elected a senior member in the Canadian Medical Association at the Toronto meeting last June, died on February 13. Dr. Turnbull was born on a farm near Barrie on March 5, 1880. He attended the local primary school and then Galt Collegiate, beginning and ending his day like so many farm boys with work on the farm. He studied at McGill from 1901 to 1905, graduating with his M.D., C.M. After two years of internship at the Verdun Protestant Hospital and a further year studying anatomy at the Montreal Western Hospital, he married Alexina Margaret Ross in 1908 and established his practice in Elmvale. This was a real horse and buggy practice, where the doctor kept two or three horses and never went out without his wire cutters for the fences. In February 1912 Dr. Turnbull went to Barrie where he had practised ever since, setting a fine example in ethics and medical skill. Dr. Turnbull served for some 40 years on the Simcoe County Medical Society Executive and was a member of the Ontario Medical Association Executive and its committees. In 1944 he was awarded life membership in the Ontario Medical Association; in 1952 he received the Bryden Award for the Ontario Medical Association District No. 5, and in 1954 he received a presentation from the County Society. Our sympathies go out to his family in their great loss.

PROVINCIAL NEWS

BRITISH COLUMBIA

Dr. G. H. Stevenson, psychiatrist heading a special Vancouver Community Chest Committee, spoke before a committee of the British Columbia Legislature which is studying the narcotics problem of this Province.

There has been a considerable body of opinion which urges the formation of narcotics clinics, where the addict would get free drugs—the idea being that they would thus be under control, and the drug trafficker would be put out of business. Dr. Stevenson spoke strongly against this suggestion, and made it clear that he opposes it absolutely; he gave sound reasons for this. He said that the emphasis should be on psychiatric treatment.

Dr. Myron M. Weaver, retiring Dean of the Medical Faculty of the University of British Columbia, speaking of the future of the Medical School, made it clear that the University plans a Medical Faculty, including a 400-bed University Hospital to be built on the campus and to be operated under University control. Construction of this hospital will make larger classes possible. We understand that this is officially the policy of the governing body of the University.

Dr. Weaver suggested that a course on the history of medicine should, in some way, be fitted into the curriculum.

President Norman A. MacKenzie paid a cordial tribute to Dr. Weaver's work in the organizing of the Medical Faculty, and in medical education in Canada generally and British Columbia.

Burnaby General Hospital is to be enlarged by a 125-bed addition. Construction is expected to begin soon. Hospital occupancy averaged 99.5% at one time and the need for more accommodation is urgent.

The B.C. Division of the Canadian Red Cross held its 37th Annual Council recently in Vancouver. Mrs. J. H. Mawer, president, reported progress and achievement for 1955.

In 1955, 5,439 pints of blood were donated through 371 clinics throughout the province, nearly 22,000 pints being collected in the Vancouver area.

An interesting point made in this address was that over the eight years since the present method of collecting blood free of charge was instituted (the hospitals and

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all concerned also administering it without cost to the patient) some 370,562 pints of blood have been donated. This, with the cost of administration etc., amounts to a gift of $9,264,000 to the people of B.C. during that time.

Other activities of the Red Cross are many, including hospital visiting, Red Cross Lodges, and arts and crafts therapy. There are now nine outpost hospitals in B.C., one having been added during 1955, at Masset. These small emergency hospitals had 35 inpatients and 4,326 outpatients last year.

Home nursing, women's work committees, and disaster services are all busy departments and growing in volume and efficiency of work.

The B.C. Heart Foundation, recently organized in British Columbia, has started a drive to raise $50,000, to be applied to research and other activities in the community dealing with heart disease. Dr. G. F. Strong, recent president of the Canadian Medical Association, was largely instrumental in organizing the Foundation and is on the Board of Directors.

An important project has been under way at the University of British Columbia for the past five years, under the leadership of Dr. Paris Constantinides, Associate Professor in the Anatomy Department. This is research into arteriosclerosis, and especially the matter of cholesterol deposits in arteries. The project was undertaken with funds supplied by the American Life Insurance Foundation for Medical Research, and by the National Research Council of Canada.

Dr. Constantinides has been working with fat-splitting agents, which he has reason to hope will be successful in treatment of arteriosclerosis associated with high blood fat levels. He has been able to arrest the development of arteriosclerosis in experimental rabbits—and even has seen indications of regression in the fatty material lining the arteries, despite continued feeding with high fat diets. The substances used by him—sulfonated polysaccharides—were produced synthetically by the Chemistry Department of the University of British Columbia.

Dr. Constantinides points out that it will take at least two or three years of careful testing before any clinical trials in human beings can be undertaken.

A notable gift by a private benefactor has recently been made to the Royal Columbian Hospital of New Westminster by James G. Robson, a prominent B.C. lumberman. The gift was $100,000, and is intended by the donor to be devoted to a nurses' home and training school. This munificent gift on the part of Mr. Robson will greatly help the Board of Directors of this growing hospital. Plans have been made for this school, which will cost $1,600,000, half the sum being paid by the city and the rest being made up from various sources.

Mr. Robson is a very prominent community worker in New Westminster and has served on the Park Board and in other capacities. J. H. MACDERMOT

Editorial Note:

Our very faithful correspondent from Vancouver, Dr. J. H. MacDermot, has been the recipient of a delightful and well-deserved tribute from B.C. physicians. He has for 24 years edited the *Bulletin of the Vancouver Medical Association*, and the executive of this association decided recently to honour him at a testimonial dinner at the Vancouver Club to which the Princes of Good Fellows, Osler lecturers, and editorial board were invited. In addition the board prepared, unknown to Dr. MacDermot, a special issue of the *Bulletin*, containing a series of tributes paid to him at the dinner. From these, we select the closing remarks of Dr. Wallace Wilson, as typical of general opinion: "We who have lived through the years with Dr. MacDermot know him for what he is and what he has done and it is but fitting that we salute him tonight and that we should record the fact that he has no enemies and innumerable friends." S.G.

SASKATCHEWAN

Arrangements have been completed for a refresher course in pædiatrics and obstetrics to be held April 5, 6, and 7 at the Regina General Hospital. The course has been planned so that it will be of particular interest to general practitioners in country points, doing both maternity and pædiatric types of practice, and will consist of papers, panels and open question periods.

Provincial government grants totalling $72,750 to four hospitals have been announced by the Honourable T. J. Bentley, Minister of Public Health. St. Joseph's Hospital at Estevan will receive $48,000 toward construction of a modern 34-bed wing, and improved outpatient and diagnostic facilities. A grant of $16,000 has been approved for the construction of a new 16-bed hospital at Davidson. A total of $5,000 has been granted to assist the Indian Head Union Hospital Board in improving medical facilities at Fort Qu'Appelle for a new health centre.

A grant of $3,750 has been approved for the construction of a nurses' home at Climax.

The prairie provinces' Regional Meeting of the American College of Physicians was held at the Bessborough Hotel, Saskatoon, on Friday and Saturday, February 3 and 4. All fellows and associates of the college were invited to attend, as well as other local members of the medical profession.

The scientific programme was prepared under the chairmanship of Dr. D. M. Baltzan of Saskatoon. The highlight of the meeting was the attendance of Dr. Walter L. Palmer of Chicago, President-Elect of the College. He was the guest speaker at the dinner on Friday evening, his topic being the "Educational Purposes and Activities of the College". Dr. Baltzan presided at the dinner.

Dr. C. H. E. Walton, Governor for Manitoba and Saskatchewan, presided at the opening session on Friday morning, and Dr. Percy Sprague, Governor for Alberta, presided at the afternoon session.

Dean J. F. Leddy, from the College of Arts and Science of the University of Saskatchewan, addressed the luncheon on Friday, his topic being "The Humanities". The presiding officer at the luncheon was Dean J. W. Macleod of the College of Medicine.

Friday's session was held at the Bessborough Hotel and the Saturday morning meeting, which concluded the conference, was held at the University Hospital.

The Saskatchewan Government Air Ambulance Service has completed 10 years of successful operation and has logged over 2,254,000 miles. The scheme was inaugurated during the height of a southern Saskatchewan blizzard in February of 1946, and the service as of the year of 1955 has completed 3,617 continuous days of providing emergency service.

There are air ambulance services operating in Australia and New Zealand, which carry the physician to the patient. So far as we are aware, Saskatchewan is the only area where the reverse is true.

The initial cost of the service, with one Norseman aircraft and a pilot-nurse team, was estimated at about $75,000. Today the service has increased to 4 Cessna 195's, one twin-engine Beechcraft, four pilots, four registered flight nurses, six aircraft maintenance experts, a radio technician, stock clerk and a caretaker, and much specialized equipment. Mr. D. N. Campbell, a former ambulance pilot, now acts as chief pilot and supervisor of the service.

The Air Ambulance Service operates as a non-profit organization, and, in spite of increased costs, the rates have been placed at a nominal fee of $25 per patient and a $10 fee per passenger, regardless of the distance covered in the boundaries of Saskatchewan. Outside the province the fees are 35c per patient mile, both ways, and passengers at 7½c per mile.

14 different symptoms in 14 different patients

pointed to a single diagnosis—depression

Watts[1] saw varied, ill defined, and apparently unrelated symptoms—such as the ones below—in 14 of his patients:

insomnia—
fainting—
pain in chest—
indigestion—
fatigue—
dizzy spells—
cough—
asocial behavior—
fear of being alone—
weeping bouts—
loss of interest in job—
irritability—
chronic invalidism—
heavy drinking.



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At first the service operated only from its Regina headquarters, and covered all the populated Saskatchewan area, but to avoid covering unnecessary territory the Saskatoon base was opened as an auxiliary base in May 1952. Under this new system the Regina crews look after the southern part of the province and out-of-province flights, while Saskatoon takes over the north central districts. Because the service has no facilities in the far north, aircraft companies operating in that area, such as the Saskatchewan Government Airways, look after northern patient flights.

Northern patients requiring treatment in southern Saskatchewan are picked up by a non-air-ambulance aircraft, and transported to a northern airport where an air ambulance plane picks them up and flies them to their destination.

Although air ambulance aircraft land almost anywhere and anytime, there are some cases where the service objects to landing in pastures or farmyards. Owing to spring breakups where there is not enough snow for skis and the ground is too soft for wheels, a ban is temporarily placed on all landings except airport to airport calls, making it necessary for patients to be transported to the nearest licensed airport before being picked up by the air ambulance.

When rural fields begin to dry off, the parties requesting a trip are asked to drive an automobile in a straight line and in high gear the full length of a one-half mile field. If this can be successfully completed, an aircraft will immediately be dispatched from one of its two Saskatchewan bases.

Construction in various communities of landing facilities for aircraft has taken place and is evidence of the fact that the people of Saskatchewan are becoming aware of the service's importance. These small strips make landings and takeoffs easier as well as speeding up the process of getting emergency cases into hospitals.

The College of Medicine, University of Saskatchewan, is offering a refresher course for general practitioners who wish to attend on April 23, 24 and 25. A small registration fee will be charged. The course will be held at the University Hospital. It is intended to discuss the following subjects at the course: diabetes mellitus and some of its complications; the subject of hyperthyroidism will be discussed from the standpoint of diagnosis and medical treatment and the associated problems in anæsthesia; a panel discussion will take place in which a physician, a surgeon, and a physician from the Department of Therapeutic Radiology will participate; a half-day is being given over to the subject of low back pain and sciatica, and it is also the intention to deal with the cervical disc syndrome and shoulder-hand syndrome in the same morning; one half-day will be given over to the subject of farm accidents and their treatment; another half-day will be given to the subject of the fluid balance in pre- and postoperative treatment. It is hoped that many physicians will be able to attend.

A cancer symposium is being planned for Regina during May 17 to 19, 1956, sponsored by the Canadian Cancer Society, Saskatchewan Division. It will be presented by the medical staff of the Allan Blair Memorial Clinic. Distinguished speakers from outside points are being invited.

QUEBEC

McGill University is the recipient of a grant reported to be the largest of its kind ever made by Britain to a Canadian institution. The Wellcome Trust of London, England, has donated $140,000, to be paid over a period of five years, to support anæsthesia research at the university and its teaching hospitals. This will make possible the appointment of a full-time research professor of anæsthesia as well as appreciable extension of research activities in this field. No doubt this comes as recognition both of the growing importance of anæsthesia and the pioneer work of Dr. Wesley Bourne, who established the department at McGill in 1946, and that of his successor, Dr. Harold Griffith, the present head of the department.

Dr. Gilles C. Lorange of Montreal has received a fellowship from the Canadian Cancer Society. A graduate of the University of Montreal, Dr. Lorange has been carrying on postgraduate studies at Bellevue Hospital in New York for the past few years. This fellowship will enable him to continue studies in chest diseases in England and Sweden.

Some time ago our Division tendered an invitation to the World Medical Association to hold its 1959 Annual Meeting in this province. It is now learned that this invitation has been accepted and the meeting will take place in September 1959, probably in Montreal.

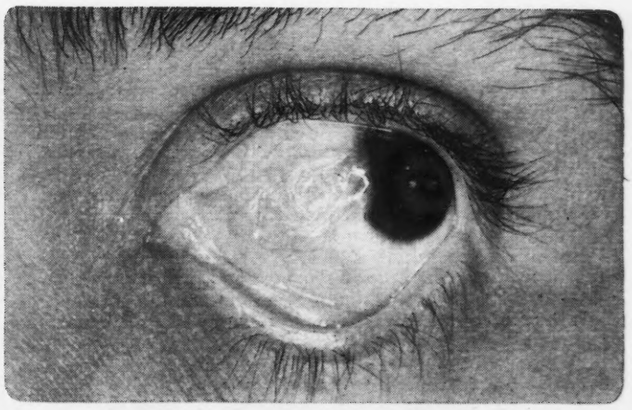
Under joint sponsorship of the Montreal Physiological Society, the Montreal Neurological Society and the Montreal Cancer Club, Dr. Paul Weiss of New York delivered a special lecture at the Montreal General Hospital on Monday, February 6. He spoke on prospecting in the field of growth and differentiation, based on research carried out during a number of years. He presented an experimental and theoretical analysis of growth and differentiation in animals. Dr. Weiss was formerly Professor of Zoology at the University of Chicago, and is now Director of the Section on Developmental Biology of the Rockefeller Institute for Medical Research.

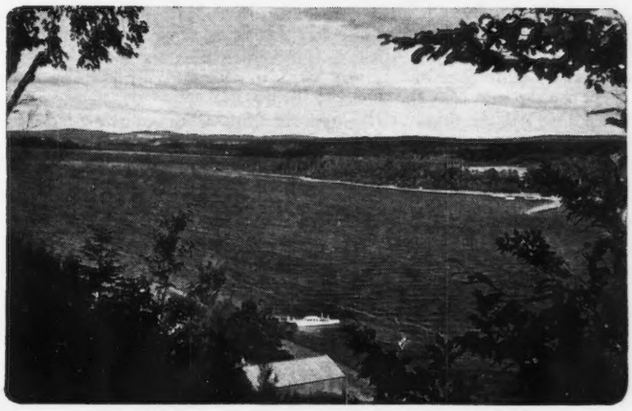
Dr. Edward W. Lowman, director of the Institute of Physical Medicine and Rehabilitation, Bellevue Medical Center, New York University, delivered the annual Dandurand-Wright Memorial Lecture to the Canadian Arthritis and Rheumatism Society, Quebec Division, in Montreal on February 8. He emphasized that in the last 50 years the population in the United States has increased 85%, but the number of chronic disease victims by 200%. Ten million people at present suffer from some type of rheumatism. Generally, these diseases can not be cured, but many of the patients can be successfully rehabilitated to a useful life. The job, however, can only be done by a team. The arthritic needs many services which can best be provided in clinics so that the patient is not hospitalized or confined to home.

Dr. Lowman's institute recently completed the fourth year of a five-year pilot study on 38 persons severely disabled by arthritis. In this study these people are given carefully planned medical and rehabilitation treatments. After two years, 22 were discharged as completely self-sufficient, 12 were discharged as partially rehabilitated, and four remained in hospital. Of the 22, eight have obtained employment. This, however, does not include housewives who maintain a home and family. Several others do part-time work at home. Dr. Lowman emphasized that this proves that properly selected patients can reverse their disability to become productive members of society again. He warned that the community must assume its responsibilities if chronic disease victims are to be returned as productive members of society.

The Department of Psychiatry at McGill University has introduced this year a new feature into the teaching programme for undergraduate students in medicine. Through the session the departments of psychiatry of each of the teaching and affiliated hospitals put on lecture-demonstration evenings for all second, third and fourth year students. The emphasis is to familiarize students with available psychiatric facilities and treatment procedures. Your reporter attended one of these sessions, at Queen Mary Veterans Hospital on February 9. The full group first gathered in the auditorium of the hospital at 7:30 p.m. The director of psychiatry, Dr. T. E. Dancey, briefly outlined the function of

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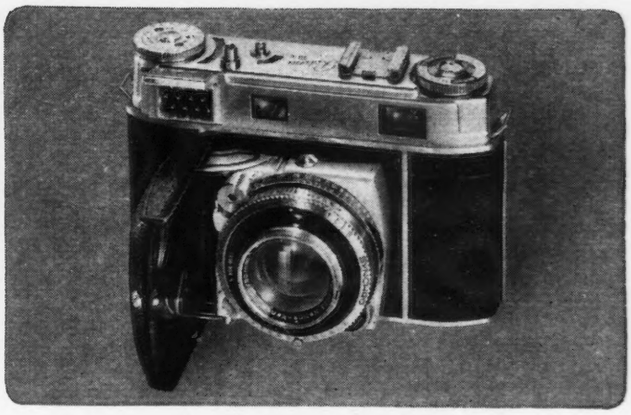




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Department of Veterans Affairs—Department of National Defence hospitals, the psychiatric treatment programme and the resident training programme. A special visitor that evening, Brigadier John Crawford of Ottawa, spoke briefly on postgraduate training in the Armed Forces. Then followed group demonstrations of facilities and treatments in this hospital, with brief case presentations. The programme terminated with refreshments. All the resident and consulting staff in psychiatry at this hospital participated in this lecture-demonstration, with Dr. Allan Mann as chairman. No doubt this is an attempt to arouse greater interest in this newer specialty at the undergraduate level, a very commendable study.

The following nominations are announced from the Faculty of Medicine of Laval University. Dr. Renaud Lemieux, President-elect of the C.M.A., is appointed Head of the Department of Medicine of the Faculty. Dr. Lucien LaRue, Medical Superintendent of the St-Michel-Archange Hospital, becomes Head of the Department of Neuro-Psychiatry, and Dr. François Roy is to be Head of the Department of Surgery.

The Jean Talon Hospital in Montreal, serving the north central area of the city, was opened a little more than a year ago with 94 beds and 13 bassinets. It has been operating at 95% capacity and for an estimated population of 293,000. Work is now in progress on a new wing which will bring the capacity to 120 beds and 75 bassinets. This will also extend the outpatient department facilities to handle 300 patients a day. The hospital, a member of the Montreal Hospital Council, has a medical consulting committee consisting of Drs. Antonio Cantero, Jean L. Rochefort and Norbert Bourgault.

A. H. NEUFELD

The 35th annual banquet of the Osler Society of McGill on February 28 proved to be a love-feast in the most pleasant sense of that pleasant word. Naturally, the occasion has always recalled the memory of Osler, but this year the Society widened and enriched this observance by paying a special tribute to Dr. W. W. Francis, librarian of the Osler Library. As noted in the March 15 issue of this journal (page 469), a book of tributes to Dr. Francis was prepared for presentation at the dinner, together with his portrait, and an unusually large gathering made the occasion a notable one.

The address of the evening was given by Dr. John F. Fulton, Sterling Professor of the History of Medicine, Yale University, whose frequent visits to Montreal have made him a familiar and most welcome figure. His activities in the literary and historical field have been and still are so intertwined with those of Dr. Francis that his being chosen to complete the tribute was one of those entirely happy selections which are so easy to make because they are in every way so desirable.

It was a most attractive feature of the evening that their parts in such a pleasantly complementary manner. both the guest speaker and the guest of honour played After he had overcome his very natural initial emotion at the warmth of the ovation, Dr. Francis went on to speak with his characteristic alternation of the serious and the light. The floodgates of his memory were opened and he entertained his audience with much reminiscence and humorous comment. His continual allusions to his friends sustained the atmosphere of intimacy which was so evident throughout the evening. He even sang (after carefully setting the key with a practice run!) a couple of verses from a college song of his student days.

Dr. Francis did not regard the occasion as a leave-taking, but rather, he said, as a jamboree. He said that if he had to use only two Latin words for the occasion they would be "Nunc Dimittis". Then he quoted Landor's lines

"I warmed both hands before the fire of life;
It sinks, and I am ready to depart,"

adding immediately, however, "but I'm *not* ready to depart!"

Dr. Fulton maintained charmingly a combination of high esteem and intimate friendship. He paid tribute to Dr. Francis as a savant and a true lover of books and then drew on an inexhaustible store of reminiscences and carefully preserved correspondence to delight his audience with examples of Dr. Francis's inimitable drollery as well as of his sound scholarship. It was all done with such lack of formality and with opportunity (fully used) for interjections and even argument from Dr. Francis, that the whole scene assumed the spontaneity and attractiveness of two friends in talk.

Too much praise cannot be given to the banquet committee for their delightfully unobtrusive and graceful way of presenting bouquets of flowers to Mrs. Francis simultaneously with the presentation to Dr. Francis; to Mrs. J. F. Fulton, when her husband rose to speak; and of recognizing with a handsome bag the work of Miss Cécile Desbarats, the "hidden" but quite indispensable hand in the Osler Library.

The patron saint of the Society himself never presided over a more animated and jocund occasion.

H. E. MACD.

NEW BRUNSWICK

Dr. H. L. Logan of Sussex, N.B., District Medical Health Officer for Kings and Queens Counties, has been elected a Fellow of the American Public Health Association.

Dr. P. C. Laporte, M.B.E., of Edmundston has been appointed acting District Medical Health Officer for Madawaska County to succeed Dr. Euclide Rioux, resigned.

Dr. R. T. Hayes, President of the Advisory Board of the Institute, was chairman of the opening ceremonies of Fundy Hall, the $250,000 residence and rehabilitation centre for the blind. The new building was officially opened by Lieutenant-Governor D. L. MacLaren. Colonel A. E. Baker, Managing Director of the Canadian National Institute for the Blind, was the chief speaker.

The directress of St. Joseph's Hospital, Saint John, has announced that Dr. J. R. Nugent has been elected president of the medical board and that Dr. Samuel Milrod has been elected president of the standardization board of the hospital for 1956.

Dr. C. W. Kelly of the N.B. Department of Health addressed a meeting in Fredericton stressing the necessity of a 100% chest x-ray survey to rule out hidden sources of tuberculosis infection. Dr. H. S. Wright, Mayor of Fredericton, suggested this survey and widespread support was guaranteed by 18 organizations in that city.

At Chatham, N.B., the combined medical staffs of the Hotel Dieu and Mount St. Joseph's Hospitals elected the following officers for 1956 at the annual meeting: president, Dr. R. H. Morrisey; vice-president, Dr. J. C. Duffy; secretary, Dr. M. B. Kingston.

The Honourable Dr. J. F. McInerney, Minister of Health for N.B., represented the province at the Dominion-Provincial Health Conference. The Minister was accompanied by Dr. J. A. Melanson, Chief Medical Officer, and Dr. C. W. Kelly, Director of Health Planning.

Among items announced by the N.B. Department of Health was a new listing of notifiable diseases for the province; it was also decided to employ a full-time person to administer the programme of the newly organized Provincial Co-ordinating Body for Crippled Children.

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At the February meeting of the Saint John Medical Society, Dr. Clarence L. Gosse of Halifax was the speaker. His subject was "Prostatism". A. S. KIRKLAND

CANADIAN ARMED SERVICES

Colonel G. L. Morgan Smith, C.B.E., C.D., A.M.D. 10 (Plans and Operations), Directorate of Medical Services (Army), paid a recent visit to Fort Sam Houston, Texas, to examine medical training methods at Brooke Army Medical Center. Brooke is a huge military medical establishment including, in addition to the field training schools, a very large army general hospital. On this one station the whole cross-section of war medicine can be seen, from the training of a private soldier on entry into the service to the conduct of skilled medical research. The teaching aids are of high order, and the method of presentation of the subject material would be of great interest to any medical school. Several of the attending medical officers, in informal discussions, volunteered the information that they had not experienced such inspired teaching in any of their various universities. Advantage is taken of the excellent facilities of this medical centre to give periods of specialist training to selected officers of the Royal Canadian Army Medical Corps.

Major R. Fournier, M.D., D.P.H., of the R.C.A.M.C. returned to Canada during March from Indochina where for the past year he served as Senior Medical Adviser to the Military Component, Canadian Delegation, International Supervisory Commission. He was replaced by Captain J. W. Fortin, R.C.A.M.C. Major Fournier's post was a busy, responsible one and provided a varied and useful experience, particularly in the fields of preventive medicine and tropical diseases.

Lieutenant-Colonel William R. Slack, C.D., M.D., C.M., D.P.H., R.C.A.M.C., aged 46, Senior Canadian Officer in Korea, was killed in a jeep accident north of Seoul on February 4, 1956. A member of the non-permanent militia from 1929 to 1939, Colonel Slack, who was a graduate of Queen's University, joined the Regular Army at the outbreak of the Second World War. During a long and distinguished career he saw service overseas and later was Commandant of the Royal Canadian Army Medical Corps School at Camp Borden. At the time of his death he was Officer Commanding the Third Canadian Field Ambulance. The funeral service was held at the United Nations Cemetery, Seoul, on February 7 and a memorial service took place at St. Paul's Eastern United Church, Ottawa, on February 12. His was a dynamic personality and he will long be remembered with affection by those who served with him; our sincere sympathy goes to his widow and daughter.

The Royal Canadian Army Medical Corps has suffered a severe loss in the sudden death on January 27 of Major George Lincoln Stoker. Born in Winnipeg on November 2, 1911, he graduated from the University of Manitoba in 1935 and, after a period of internship at the Misericordia Hospital, practised first at The Pas and then in Vancouver. At the outbreak of the Second World War he joined the R.C.A.M.C. and saw service in England, Africa, Italy and Northwest Europe. In 1945 Major Stoker returned to private practice in Dawson Creek and Salmon Arm before rejoining the R.C.A.M.C. in August 1949. He served in Korea, and at the time of his death was Officer Commanding, Shilo Military Hospital. This outstanding officer and doctor, who had special talents as a surgeon, will be sadly missed and the sympathy of the entire medical corps goes to his widow.

BOOK REVIEWS

SPLENIN A IN RHEUMATIC FEVER. A. F. Coburn, L. V. Moore, J. Wood and M. Roberts, The Rheumatic Fever Research Institute, Northwestern Medical School, Chicago. 87 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1955. $4.00.

Dr. Coburn and co-workers have had long experience with rheumatic fever, and any study or conclusion they present merits thoughtful consideration.

Splenin A is an extract of the spleen originally described by Karjala and was used for a clinical trial in 47 children with acute rheumatic fever. It appeared to have a temporary anti-inflammatory action in most of these children. In 10 cases the signs of heart disease disappeared over a period of three years. No controls were set up, so no conclusion can be drawn in this regard.

Further investigation is needed to understand more fully the factors involved in the action of Splenin A. The difficulty and cost of the procedure for making Splenin A preclude its use on a large scale at the present time.

SPEZIELLE THERAPIE DER BLUTKRANKHEITEN (SPECIAL THERAPY IN BLOOD DISEASES). H. Goldeck, Director of the Second Medical University Clinic and Polyclinic, Hamburg. 235 pp. Illust. Ferdinand Enke, Stuttgart, 1955. Paperbound 32 marks, clothbound 35 marks.

This monograph on the special therapy of blood disorders gives a very comprehensive and objective view of the field. Dr. Goldeck, after a preliminary chapter on the pathogenesis of anæmias, describes the individual measures which may be taken to treat the anæmias and then considers in detail the treatment of the various types. In the second part of his book, he discusses the therapeutic possibilities in the malignant disorders of the blood, dealing with the various cytostatic agents from urethane on, as well as radiation therapy, and again giving detailed instructions for treatment of the different diseases involved. A short part of the book deals with the hæmorrhagic diatheses and the book closes with various suggestions for treatment of bone marrow insufficiencies. There is a glossary of proprietary preparations, but this applies only to those produced in Germany. There is also a very extensive bibliography, and the whole book bears evidence of wide study of the Anglo-Saxon literature as well as other European sources.

THE THYROID. A Fundamental and Clinical Text with Sixty Contributors. S. C. Werner. 789 pp. Illust. Paul B. Hoeber, Inc., New York, 1955. $20.00.

The introduction of a book into a field of clinical medicine today requires considerable justification: there is already a profusion of books in the thyroid field in particular, and the Quarterly Cumulative Index Medicus lists nearly 8,000 references to the thyroid in the past decade. The editor has recognized the need to sift and appraise this mountain of literature, and to bring forth in one volume a résumé of this work. He has enlisted the talent of 60 eminent contributors, each of whom has evaluated an aspect of the subject in his particular sphere of interest and experience. There has been an admirable and close blending of the worlds of the clinician and the investigator.

The book is divided into three parts. Part I deals with the fundamental aspects of thyroid function in man, the mechanisms which construe the activity of the gland, the biochemistry of the hormone, and the histology and comparative anatomy of the gland.

Part II presents the laboratory methods which supplement the clinical appraisal of thyroid secretory activity.

Part III considers diseases of the thyroid. A major goal throughout the volume has been to assess the validity of

the facts on which current information or procedure is based. The information is documented in most instances, and the references have been carefully selected. This latter deserves special emphasis, since too often the reader is sacrificed to the writer's sense of completeness as regards references. Such lists become useless since the contributor's ability to edit the literature and thus guide the reader is wasted.

The book is well organized and easily readable. The type is large and clear, and the book has been well bound.

This would be a very worthwhile addition to the library of any clinician or research worker whose interests touch on this subject. For those particularly interested in this field, it would be difficult, if not foolish, to do without it.

PRINCIPLES AND PRACTICE OF ANTIBIOTIC THERAPY. H. Welch and others. 600 pp. Interscience Publishers, Inc., New York, 1954. $12.00.

This is an extremely comprehensive and authoritative review of the use of present-day antibiotics. Although it is written by a number of contributors the style is surprisingly uniform and easy to read. The advice given is definite and detailed. The first part of the book includes descriptions of the pharmacology, toxicity and dosage of the individual antibiotics and is a mine of fundamental information which clarifies the understanding of these substances and the indications for their use. The last half of the book consists of a discussion of the management of various specific types of bacterial infection in various clinical situations. Frequent new editions have been necessary to keep up with the rapid changes in this field of medicine, and the present book is extremely up to date and useful.

TOPLEY AND WILSON'S PRINCIPLES OF BACTERIOLOGY AND IMMUNITY. G. S. Wilson, Director of the Public Health Laboratory Service, England and Wales, and A. A. Miles, Professor of Experimental Pathology, University of London. 4th ed. Two vols. 2,330 pp. Illust. Edward Arnold, London; The Macmillan Company of Canada Limited, Toronto, 1955. $27.00.

The publication of a new edition of Topley and Wilson is of international interest to bacteriologists, for no other textbook in the English language on the subject occupies so pre-eminent a position.

Like the third edition, which appeared in 1946 and was twice reprinted, the present edition is in two volumes, edited by Dr. G. S. Wilson and Professor A. A. Miles. The revision of the text has been far-reaching and thorough. There are few deletions and many additions, making 277 additional text pages.

In the systematic section there are now 304 species of *Salmonella* compared with 140 previously named. Extensive additions have been made in the chapter on bacteriophage. The chapters on filtrable viruses and virus diseases have been greatly enlarged, as has the chapter on chemotherapeutic drugs and antibiotics. Much new work has been introduced on morphology, bacterial metabolism, food poisoning and tuberculosis. Some topics are either mentioned for the first time or given more extensive emphasis, such as sarcoidosis, cat-scratch fever, infectious hepatitis, and pinta.

The list of references contained at the end of each chapter is remarkable, some having as many as 10 pages and more. This is a very valuable feature of the work, for not only will the reader find the desired information in the text, but if he requires more or disagrees with the authors' interpretation the source of the information is immediately available to him.

In the preface the authors themselves say that parts of their text have now too many details for the undergraduate medical student. They have for that reason incorporated more detail and more references in order to ensure that the book is of greatest value to those for whom it was primarily intended—postgraduate students, research workers and university teachers.

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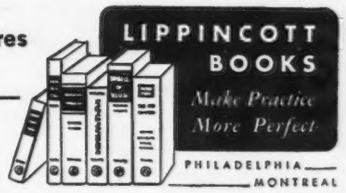
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April 1, 1956, vol. 74

MALADJUSTED CHILDREN. C. C. Burns, Senior Psychiatrist to the Birmingham Child Guidance Service, Birmingham, England. 80 pp. Hollis & Carter, London; International Publishers Limited, Montreal, 1955. $1.50.

The author of this book for the laity has produced a wise and interesting work on the maladjusted child. Although he writes from the Catholic standpoint, his book is based on general Christian values and can well be read by those not of his Church. To demonstrate briefly the author's viewpoint and to indicate the public it is addressed to, we cannot do better than quote from his opening chapter.

"The need for understanding, tolerance, and tenderness is a desperate one in our days; we cannot afford, any of us, to have rigid, puritanical, or punitive ideas with regard to human relationships. We need a deep human pity as well as a belief in the infinite mercy of God. There is danger in too much rectitude; in that kind of cold 'charity' which finds it necessary to *force* children to be good, to be obedient, to be religious: with no real understanding, no warmth, no sympathy. It is terrible when sensitive children are punished or shamed, unjustly or stupidly, often from sheer lack of imagination.

"If this book is aimed at anyone in particular, it is at those men and women, lay and religious, who are dealing with deprived, delinquent and maladjusted children, in schools and institutions of all kinds. I hope however that it may rouse a social and psychological conscience in others . . . "

As an introduction to the subject, this book is recommended.

THE CANADA YEAR BOOK—1955. The Official Statistical Annual of the Resources, History, Institutions, and Social and Economic Conditions of Canada. Dominion Bureau of Statistics, Canada Year Book Section, Information Services Division. 1,374 pp. Illust. Queen's Printer and Controller of Stationery, Ottawa, 1955. $3.00.

In addition to the regular textual and statistical material, the 50th anniversary edition of the Canada Year Book includes, in its chapter on "Public Health, Welfare and Social Security", the preliminary results of the Canadian Sickness Survey, conducted in 1950-51 by the Dominion Bureau of Statistics and the Department of National Health and Welfare with the co-operation of the provincial departments of health. Data from the survey include estimates of the volume of sickness during the survey year, estimated volume of physicians' and dentists' services, and classification of family expenditures for health care. Other sections of this chapter review federal health activities (including the National Health Grants Programme), provincial and municipal health activities, hospitals, and public welfare and social security programmes.

A DOCTOR'S BOOK OF HOURS. M. Moore. 397 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1955. $6.50.

Those who have been exposed to the poetry of Merrill Moore will know what to expect in this latest collection of poems. Dr. Moore is a physician in Boston who spends his spare time in writing poetry, mostly in sonnet form. Quite a lot of poems stem from observations on patients; some of the observations are hardly flattering, but remarkably entertaining. Dr. Moore also comments on a wide variety of subjects which have come to his mind as a result of the practice of his profession. Those who have never sampled his wit would be well advised to have a look at the book before purchasing it. It is our prediction that in many cases a taste for Dr. Moore will rapidly develop and the purchase will be made.

THE BOKE OF CHYLDREN. Thomas Phaire. 76 pp. Illust. E. & S. Livingstone Ltd., London and Edinburgh; The Macmillan Company of Canada, Limited, Toronto, 1955. $1.30.

In 1545 Thomas Phaire, then resident in Pembrokeshire, wrote the first textbook of pædiatrics in English. A specimen of the 1553 edition of this work, *The Boke of Chyldren*, is in the Medical Library of the University of Bristol, England, and two West Country pædiatricians have now reproduced this edition with a glossary and introduction.

This slim volume would make an excellent present for anyone interested in diseases of children, for Phaire has a charming style and his book is full of quotable phrases. He has a tilt at the critics "whiche wyl doo nothyng but detract and iudge other, snuffying at al that offendeth the noses of their momish affections" and defends his use of the English language—"why grutche they phisyke to come forth in Englyshe? Woulde they have no man to know but onely they?", and chides the pessimistic pædiatrician, "for somuche as many do suppose that there is no cure to be ministred unto them [children] by reason of their weakenes".

Thomas Phaire has insight into matters not commonly understood in his day, as when he points out that epilepsy is "Sometyme by nature receyued of the parentes" and that in measles and smallpox "the best and moste sure helpe is not to meddle with anye kynde of medicines, but to let nature worke her operacion". His therapeutic remedies of course range all the way from ground-up earthworms to opiates (syrupe of popye) for insomnia. His book is recommended to anyone with even a slight interest in medical history.

GERMAN-ENGLISH MEDICAL DICTIONARY. W. O. Goulden, Cologne University, Germany. 513 pp. J. & A. Churchill, Limited, London, 1955. $7.75.

At the end of World War II there was a crying need for a good German-English medical dictionary. Lang and Meyer was out of print, and nothing new had appeared for some years. Ten years later, the situation has changed somewhat, for several lexicographers have attempted to fill the gap. Any new dictionary is therefore liable to closer scrutiny than would have been the case ten years ago.

Dr. Goulden's dictionary contains some 50,000 entries, and is fairly sharply focused on the medical sciences. Its general standard of accuracy and comprehensiveness will make it suitable for those whose German is defective and who need to read papers in German journals. No dictionary is perfect, and the present one has a number of blemishes, in part probably due to the fact that the author is not a practising clinician. Thus a *Zinkleimverband* is not usually a zinc oxide dressing but an Unna's paste dressing. English practitioners may not recall that Feer's disease is a synonym for pink disease, or Biermer's anæmia a synonym for Addisonian anæmia. There is some confusion over the word *Eiweiss*, which in most entries is translated as albumin whereas in the majority of cases in medical texts it means protein. Thus *Eiweisskörper* is a protein, not an "albumin particle", *Eiweissmangelkrankheit* means protein deficiency disease not "disease due to albumin deficiency" and so on.

The proofreading could have been stricter (osteomyelitis is spelt three different ways on page 222), but this is a common complaint nowadays.

On the whole, in spite of these criticisms, the dictionary may be regarded as quite adequate for its purpose, though the advanced medical translator will continue to sigh for perfection.

Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Handbook of Medical Library Practice. Edited by Janet Doe and Mary Louise Marshall. 2nd ed. 601 pp. American Library Association, Chicago, 1956. $10.00.

Polymyxin, Neomycin and Bacitracin. E. Jawetz, Professor of Microbiology, University of California. 90 pp. Interscience Publishers Inc. New York, 1956. $4.00.

Liproproteins in Serum, from Normal Persons and from Patients with Chronic Liver Diseases. I. L. Marner, Faculty of Medicine, University of Copenhagen, Denmark. 183 pp. Illust. The Scandinavian Journal of Clinical and Laboratory Investigation, Oslo, 1955.

Tuberculosis in the Army of the United States in World War II. E. R. Long, Director, Henry Phipps Institute, University of Pennsylvania, Philadelphia; S. Jablon, Statistician, Follow-up Agency, Division of Medical Sciences, National Research Council, Veterans Administration Dept., Washington, D.C. 88 pp. Illust. 1955. $1.50.

Report of the Committee of Enquiry into the Cost of the National Health Service. 309 pp. Her Majesty's Stationery Office, London, 1956. 9/-.

Introduction to Hepatic Surgery. H. Gans, Surgical Resident, Cincinnati, Ohio. 265 pp. Illust. Elsevier Publishing Company, Amsterdam; Burns & MacEachern, Toronto, 1955.

A Follow-up Study of World War II Prisoners of War. B. M. Cohen, National Research Council, Washington, D.C., and M. Z. Cooper, Veterans Administration, Washington, D.C. 81 pp. Illust. Veterans Administration Dept., Washington, D.C., 1954. $1.50.

The Cost of the National Health Service in England and Wales. B. A. Smith and R. M. Titmuss. 176 pp. Cambridge University Press, London; The Macmillan Company of Canada Limited, Toronto, 1956. $4.70.

Christopher's Textbook of Surgery. Edited by L. Davis, Chairman of the Dept. of Surgery, Northwestern University, Chicago. 6th ed. 1,484 pp. Illust. W. B. Saunders Company, Philadelphia, 1956.

Cardiovascular Innervation. G. A. G. Mitchell, Professor of Anatomy, University of Manchester, England. 356 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Ltd., Toronto, 1956. $9.35.

Outline of Orthopædics. J. C. Adams, Consultant Orthopædic Surgeon, St. Mary's Hospital, London, England. 423 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Ltd., 1956. $5.50.

Modern Treatment Year Book 1956. Edited by Sir C. Wakeley, Senior Surgeon, King's College Hospital, London. 344 pp. Illust. The Medical Press, London; The Macmillan Company of Canada Ltd., Toronto, 1956. $4.25.

A Handbook of Medical Hypnosis. G. Ambrose, Consultant Psychiatrist, Park House Approved School, Guildford, England; and G. Newbold, Member of the Society for Clinical and Experimental Hypnosis, New York. 255 pp. Baillière, Tindall and Cox, London; The Macmillan Company of Canada Ltd., Toronto, 1956. $3.60.

Radium Therapy. C. W. Wilson, Principal Physicist to the Westminster Hospital, London. 286 pp. Illust. Baillière, Tindall and Cox, London; The Macmillan Company of Canada, Ltd., Toronto, 1956. $6.35.

The Compend. A Compendium of Ethical Proprietaries used in Medicine and Pharmacy. W. Hetherington, Chief Pharmacist, Bristol General Hospital, England. 676 pp. John Wright & Sons, Ltd., Bristol; The Macmillan Company of Canada Ltd., Toronto, 1955. $5.50.

Current Therapy. Edited by H. F. Conn. 632 pp. W. B. Saunders Company, Philadelphia, 1956.

Thirty-Eighth Annual Report of the Chief Medical Officer to the Minister of Health and Social Services for the Year Ending March 31, 1955. Department of Health and Social Services, New Brunswick, 1956.

Yellow Fever Vaccination. Kenneth C. Smithburn, The Rockefeller Foundation, New York, and others. 238 pp. World Health Organization, Palais des Nations, Geneva, 1956. $5.00.

Diseases of the Endocrine Glands. L. J. Soffer, Clinical Professor of Medicine, State University of New York, College of Medicine, New York City. 2nd ed. 1,032 pp. Illust. Lea and Febiger, Philadelphia; The Macmillan Company of Canada Ltd., Toronto, 1956. $16.50.

Diseases of the Chest. H. C. Hinshaw, Clinical Professor of Medicine, and L. H. Garland, Clinical Professor of Radiology, Stanford University School of Medicine, California. 727 pp. Illust. W. B. Saunders Company, Philadephia, 1956.

Cancer and Common Sense. G. Crile Jr., Surgeon, Cleveland Clinic, Ohio. 118 pp. The Viking Press, New York; The Macmillan Company of Canada Ltd., Toronto, 1955. $2.95.

European Seminar on the Prevention and Treatment of Alcoholism. Selected lectures. 51 pp. World Health Organization, Palais des Nations, Geneva, 1954.

A Modern Pilgrim's Progress for Diabetics. G. G. Duncan, Clinical Professor of Medicine, Jefferson Medical College, Philadelphia, Pa. 222 pp. Illust. W. B. Saunders Company, Philadelphia, 1956.

Poliomyelitis Vaccination. A Preliminary Review. 40 pp. World Health Organization Technical Report Series No. 101, World Health Organization, Palais des Nations, Geneva. $0.30.

Lung Function in Coalworkers' Pneumoconiosis. J. C. Gilson and P. Hugh-Jones. 266 pp. Illust. Medical Research Council Special Report Series, No. 290. H. M. Stationery Office, London, 1955. 21/-.

Shock and Circulatory Homeostasis. Transactions of the 4th Conference, December 1954. Edited by H. D. Green, Professor of Physiology and Pharmacology, Bowman School of Medicine, Winston-Salem, North Carolina. 291 pp. Illust. The Josiah Macy Jr. Foundation, New York, 1955. $5.00.

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By C. W. Wilson, M.Sc., Ph.D., F.Inst.P., Principal Physicist to the Westminster Hospital, London.

Second Edition. 1956. 286 pages. Illustrated. $6.35

This important new edition takes full account of the great technical advances of recent years in the use of radium therapy and will be of value to the radiotherapist and to the hospital physicist.

A HANDBOOK OF MEDICAL HYPNOSIS

By Gordon Ambrose, L.M.S.S.A., Honorary Consultant Psychiatrist, Park House Approved School, Guildford; and George Newbold, M.B., B.S., M.R.C.S., M.M.S.A., D.R.C.O.G., D.C.H., Late Obstetrician and Gynaecologist, Orsett Lodge Hospital.

255 pages. 1956. $3.60

This new book has been written to give a general introduction to the subject to students and practitioners. It presents an objective picture of the place of hypnotherapy in contemporary medical practice, and describes many cases of a kind which can safely be treated by any interested medical practitioner.

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Manuscripts: Manuscripts of original articles, case reports, clinical and laboratory notes, and special articles should be submitted to the Editor at the C.M.A.J. editorial office, 150 St. George St., Toronto, with a covering letter requesting consideration for publication in the *Journal*. Acceptance is subject to the understanding that they are submitted solely to this *Journal*, and will not be reprinted without the consent of both the Editor and the author. Articles should be typed on one side only of unruled paper, double-spaced and with wide margins. Carbon copies cannot be accepted. The author should always retain a carbon copy of material submitted. Every article should contain a summary of the contents.

The Editor reserves the right to make the usual editorial changes in manuscripts; these include such changes as are necessary to ensure correctness of grammar and spelling, clarification of obscurities or conformity to *Journal* style. In no case will major changes be made without prior consultation with the author. Authors will receive galley proofs of articles before publication, and are asked to confine alterations of such proofs to a minimum.

Reprints may be ordered on a form supplied with galley proofs.

References: Authors should limit references to published work to the minimum necessary for guidance to readers wishing to study the subject further. They should not quote articles they have never seen, and should set out references in a numbered list at the end of the article, thus:

1. Doakes, J.: *M. J. Kamchatka*, 1: 2, 1955, giving in order: (1) Author's name and initials in capitals. Where more than three authors are concerned in an article, only the first should be named, with *et al.* as reference to the others. (2) Cumulative Index Medicus abbreviation of journal name. (3) Volume number. (4) Page number. (5) Year.

References to books should be set out as follows:

Pickwick, S., *Textbook of Medicine*, Jones and Jones, London, 1st ed., p. 30, 1955.

Illustrations: Photographs should be glossy prints, unmounted and untrimmed, preferably not larger than 10 by 8 inches. Colour work can be published only at the author's expense. Magnification of photomicrographs must always be given. Photographs must not be written on or typed on. Identification can be made by pasting an identifying legend on the back. Patients must not be recognizable in illustrations, unless the written consent of the subject to publication has been obtained. Graphs and diagrams should be drawn in india ink on suitable white paper. Legends to all illustrations should be typed separately from the text of the article. Illustrations should not be rolled or folded.

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Continued on Page 36

POST-GRADUATE COURSE IN OBSTETRICS and GYNAECOLOGY

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This course is offered by the Royal Victoria Montreal Maternity Hospital and is modelled upon the lines of that given in general surgery and will be partially combined with this latter course for general surgery, X-ray, pathology and anatomical subjects. The remainder of the course will be presented by the Staff of the Royal Victoria Montreal Maternity Hospital. A correspondence portion of the course will commence on May 1 and continue for three months. The clinical and didactic full time course will be held in the Hospital in mid-August and will last six weeks.

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Although the courses provide preparation for the higher examinations of the Royal College of Physicians and Surgeons of Canada, they are available to any graduate in Medicine who desires advanced instruction.

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POSITION VACANT.—A vacancy exists on the active staff of this English-speaking general hospital for a doctor with certification in E.N.T. or E.E.N.T. to take charge of the department. All tonsillectomies referred to the E.N.T. department. A new hospital on a new site has just been completed. For further details apply to: Administrator, Jeffery Hale's Hospital, Quebec City, P.Q.

ASSISTANT required for busy general practitioner in suburban Toronto area. Opportunity for partnership. Please write giving age, experience and religion to Box 466, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

TWO ASSISTANTS in general practice required for Northern Ontario clinic, beginning July 1, 1956. Reply to Box 584, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

WANTED.—Urologist with certification or fellowship for a group in Ontario. Apply stating experience, qualifications, starting salary expected, and include a recent snapshot if possible. Box 540, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

WANTED: ANÆSTHETIST. — Well established group in central Ontario requires services of certified anæsthetist. Write stating remuneration requirements, experience and references to Box 562, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

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EUROPEAN GRADUATE, age 44, married, experienced in general practice, internal medicine and surgery, desires association with individual, group or solo in prosperous community. Considering renting or buying. Available July 1956. Reply to Box 645, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

WANTED.—Partnership or assistantship in general practice, by European graduate (Amsterdam) 1952, age 32, single. Completing senior intern year June; writing L.M.C.C. April. Interested particularly in obstetrics-gynæcology and pædiatrics. Prefer British Columbia or Alberta. Available July 1956. Reply to Box 659, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

ANÆSTHESIOLOGIST, age 36, Canadian citizen, Canadian and U.S. trained, American Board eligible, desires position. 7 years' experience in anæsthesiology. All enquiries promptly answered. Reply to Box 640, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

WANTED by McGill graduate, married with infant family, one-two year post as company doctor in or outside Canada. Reply to Box 660, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

WANTED.—F.R.C.S. (England), eligible F.R.C.S. (Canada), married, age 32, completing chief resident appointment in June, desires association with established individual or group. Reply to Box 665, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

LOCUM TENENS.—Available for locum tenens anywhere in Ontario for month of June. Experience consists of rotating internship plus two years' pædiatrics. Reply to Box 678, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

CANADIAN, age 32, McGill graduate, 1948; eligible to write orthopædic specialty; desires position as assistant in city group. Available August 1, 1956. Reply to Box 676, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

POSITION WANTED.—English graduate, L.M.C.C., seeks opening in general practice as assistant or partner in Ontario or the Maritimes. Bilingual. 3 years' hospital and 2 years' general practice experience. Reply to Box 674, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

CANADIAN ANÆSTHETIST, age 32, married; writing certification September 1956, American board eligible; desires position with a group, clinic or on hospital staff anywhere. Available July 1, 1956. Reply to Box 673, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

U.B.C. GRADUATE, 1954, age 34, married; at present completing senior rotation internship in the east; desires association with general practitioner or group in British Columbia. Available August 1956. Reply to Box 672, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

ENGLISH GRADUATE, age 31, married; one year's teaching hospital internship, two years' general practice including one year in Canada; seeks opportunity with another practitioner or group. Special interests: pædiatrics, obstetrics and industrial medicine. Reply to Box 671, Canadian Medical Association Journal, 150 St. George Street, Toronto 5, Ontario.

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Continued on Page 39

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Dermatology, Two Weeks, May 7.

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Clinical Uses of Radioisotopes, Two Weeks, May 7.

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Applicant should preferably hold a senior degree in Ophthalmology or Oto Rhino Laryngology. Previous administrative experience preferable.

Initial appointment for three years, thereafter by mutual agreement. Salary commensurate with qualifications and experience within the range of £2300 - £3000 (Australian) per annum.

Applicants must forward to the undersigned the names and addresses of four persons of academic standing who would be willing to furnish confidential reports, together with a recent photograph and the following information:—

Name:
Address:
Date and place of Birth:
Nationality:
Sex:
Marital State:
Qualifications and dates thereof:
Present appointment:
Previous appointments with dates:
Details of War Service (if any):
Published Works:
Previous experience in (a) Administration,
(b) Oto Rhino Largyngology,
(c) Ophthalmology.
Written references (not more than four).

Further information may be obtained from the undersigned with whom applications must be lodged by 12 noon, Monday, 25th June 1956.

F. Y. Turley, Manager,
The Victorian Eye and Ear Hospital,
126 Victoria Parade, East Melbourne, C.2.
Victoria, Australia.

NEWS AND NOTES

HOSPITAL CANCER PROGRAMMES

The Committee on Cancer of the American College of Surgeons has announced that a properly functioning registry of cancer patients is a requirement for approval of a hospital's cancer programme by the College, under new regulations which are now effective.

The College programme considers a hospital's cancer activities only, and is entirely separate from the Joint Commission on Accreditation of Hospitals, which accredits hospitals on the basis of detailed studies of medical and administrative activities. The American College of Surgeons is one of five member organizations in the Joint Commission.

In a new manual for hospital cancer programmes, the College's Department of Professional Services and Accreditation has set forth the minimum requirements for approval of a cancer programme.

The requirements recognize three types of cancer programme:

1. The specialized cancer hospital providing complete service for cancer patients.
2. The general hospital conducting organized cancer clinical activities, including cancer registry, cancer consultation and treatment service.
3. The general hospital, usually small in size, which maintains only a registry of all cancer patients.

All three types of programme must be under the supervision of a cancer committee of the hospital's medical staff consisting of physicians directly concerned with the diagnosis and treatment of cancer and appointed by regularly established medical staff authorities. The duties of this committee will be to initiate, supervise and continually appraise the cancer programmes and to report to the medical staff at least once annually.

The purpose of such a registry is to maintain a continuing record of successes and failures in the management of cancer patients in every hospital seriously concerned with the treatment of this disease.

Reports are to be made regularly to the members of the hospital medical staff, so that they are repeatedly apprised of their individual and collective rates of success, thus allowing comparison with other institutions and pointing out weak spots where "shoring up" is needed.

The minimum content of the cancer registry was described as including the name and address of every patient upon whom a diagnosis of cancer is or has been previously made, with adequate identifying and diagnostic information and an abstract of the clinical record. Annual follow-up notes must be maintained as long as the patient remains alive, it is stipulated.

College requirements also specify procedures for maintaining the registry, including proper methods for obtaining the complete roster of patients with cancer, methods for adding new cases as they occur,

(Continued on page 42)

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GEIGY PHARMACEUTICALS

NEWS AND NOTES

(Continued from page 40)

and methods of developing the case abstract file.

The College cancer programme also includes detailed requirements for the complete cancer hospital, and for general hospitals maintaining cancer consultation services and cancer treatment services. Hospitals of all three types must submit reports, at least annually, showing the results obtained with cancer patients and including five-year results as they become available through continuing follow-up.

The programme is supported jointly by the College, the National Cancer Institute and the American Cancer Society.

AMERICAN JOURNAL OF DIGESTIVE DISEASES

The American Journal of Digestive Diseases—published since its founding in Fort Wayne, Indiana—has been sold to Paul B. Hoeber, Inc., New York, the Medical Book Department of Harper & Brothers, New York. The new publishers began issuing this long-established independent journal in January 1956. It will appear monthly in a new format, liberally illustrated, under the supervision of a new Editorial Board. *The American Journal of Digestive Diseases* will be edited by Dr. Henry Janowitz, Head of Gastroenterology, Mount Sinai Hospital, New York, and Dr. Maxwell H. Poppel, Head of Radiology at Bellevue Hospital, New York.

HEBREW MEDICAL JOURNAL

One of the surprises of this century has been the way in which both in Israel and the United States the Hebrew language has been adapted to scientific and medical writing. In this revival of the ancient language of the Bible, the Hebrew Medical Journal, published in New York, has played a significant part. It is now in its twenty-ninth year of semi-annual publication. The second number for 1955 contains a number of articles on various aspects of health in Israel, as well as an article commemorating the 750th anniversary of Maimonides and short articles on Jewish medicine in history, endocrinology in the Bible and the physician in Jewish law and literature. For those with a poor knowledge of Hebrew, there is a section in English.

FORUM ON ALCOHOL STUDIES

The Alcoholism Foundation of Alberta and the Department of Education, University of Alberta, are holding a medical and industrial forum on alcohol studies at the Banff School of Fine Arts, Banff, Alberta, April 2-5. The object of the forum is to bring to physicians and to representatives of business, industry and labour a broader understanding of the problems of alcoholism and abnormal drinking.

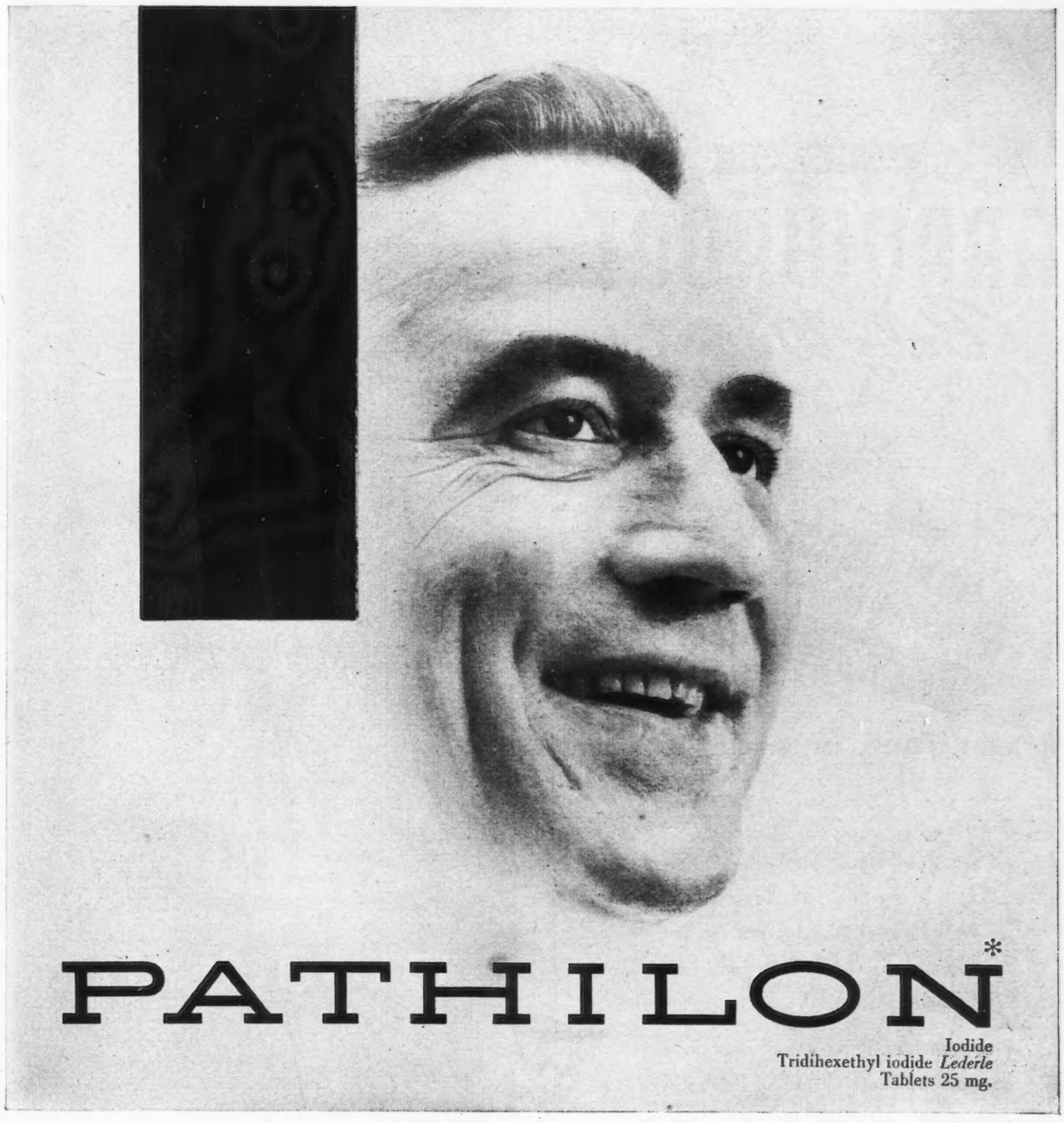
AMERICAN PUBLIC HEALTH ASSOCIATION

The 84th annual meeting of the American Public Health Association and the concurrent meetings of 40 related organizations will be held in Convention Hall, Atlantic City, N.J., from November 12 to 16. The question "Where Are We Going in Public Health?", which was examined at last November's meeting, will be reopened this year. Among the sections there is a new one on mental health. At least one day is to be devoted to the interests of the young public health worker. Enquiries should be made to the American Public Health Association, 1790 Broadway, New York, N.Y.

SEX DETERMINATION FROM VAGINAL SMEARS

Dr. Carpentier and his colleagues from the University Gynæcological Clinic, Utrecht, Netherlands (*Nederl. tijdschr. geneesk.*, 100: 154, 1956) discuss their studies of vaginal smears in 49 cases of primary amenorrhœa. They stained the smears by the Papanicolaou technique, which they consider very suitable for studying the sex chromatin. In their opinion, vaginal smears are preferable to skin biopsies or oral mucosa smears for determination of genetic sex. Smears of the urethral mucosa also proved adequate. In 45 cases, ten patients were found to be genetically male and 35 female.

(Continued on page 47)



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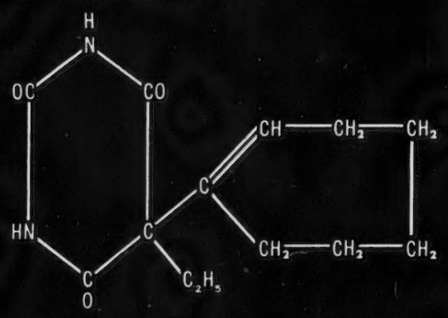
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Chemically distinctive, Medomin alone among the clinically-used barbiturates has a 7-member ring introduced into the barbiturate radical.



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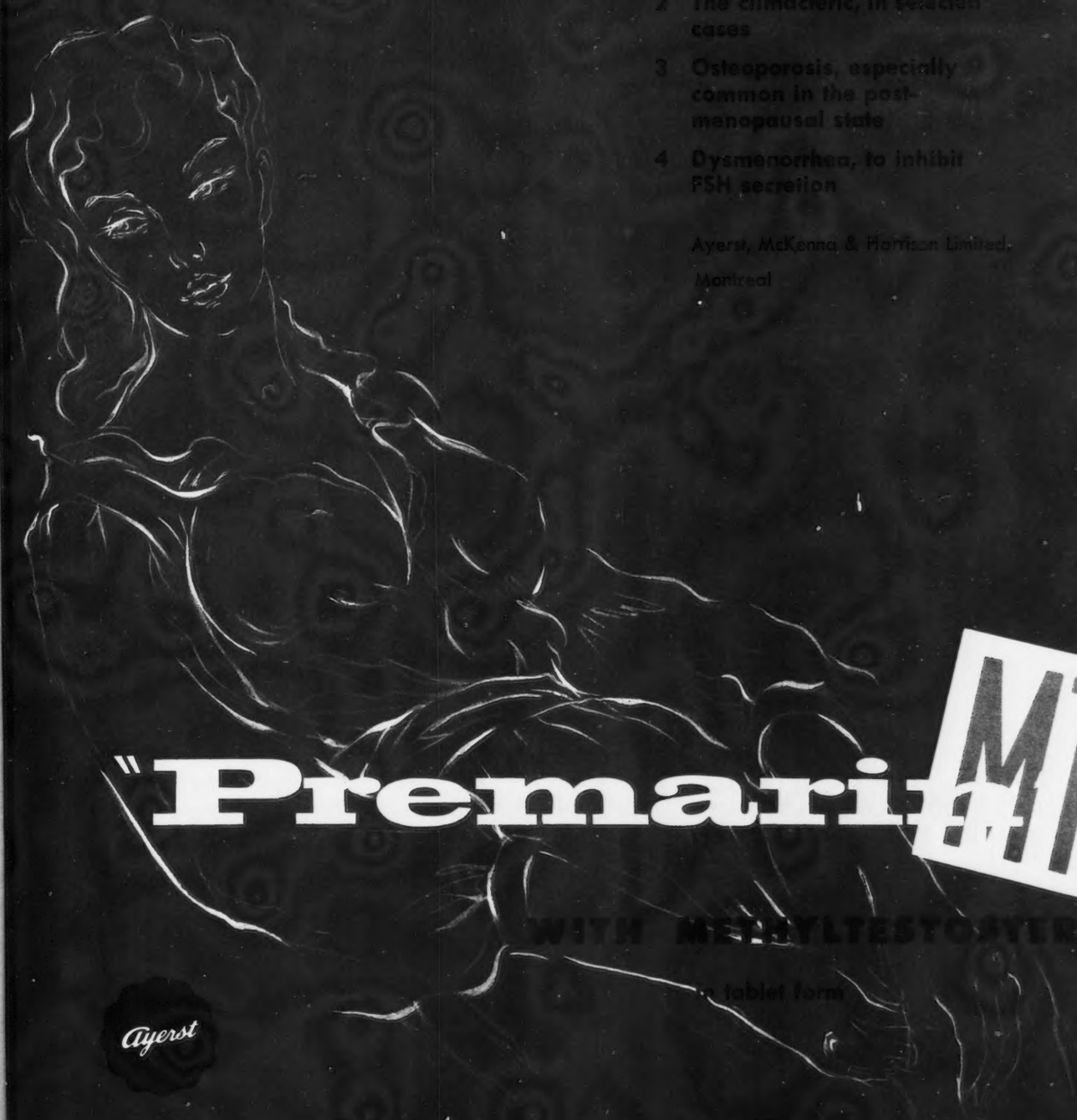
1 Prevention of postpartum breast engorgement and mental depression

2 The climacteric, in selected cases

3 Osteoporosis, especially common in the post-menopausal state

4 Dysmenorrhea, to inhibit FSH secretion

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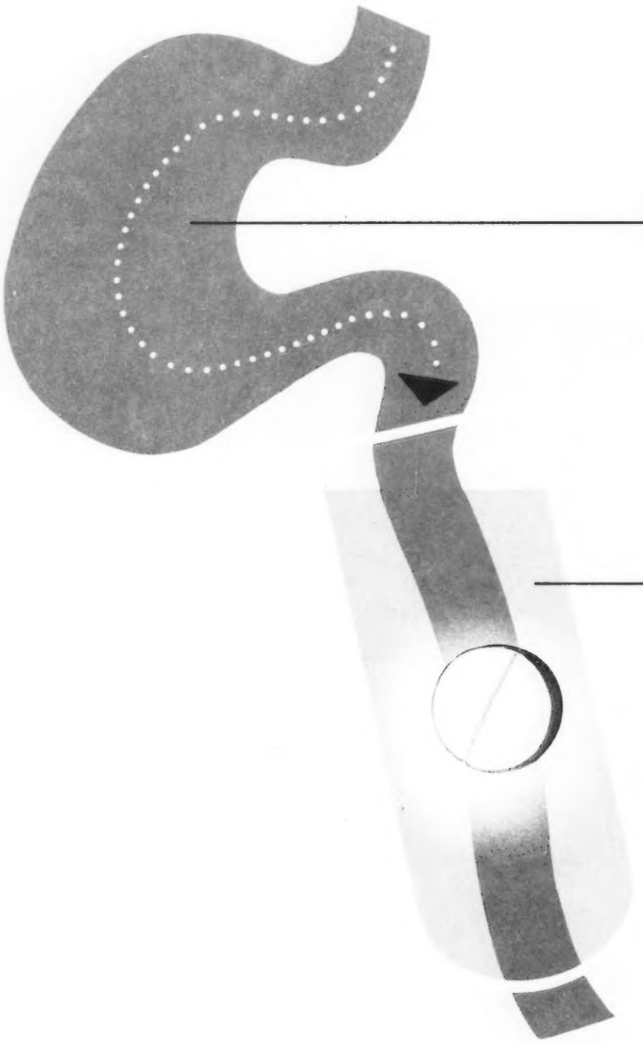


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NEWS AND NOTES

(Continued from page 42)

CREAKING JOINTS

Drs. Hunter and Brooks of Toronto (*J. Lab. & Clin. Med.*, 47: 289, 1956) record some interesting work on noise in human joints. They mention that attempts to study joint diseases by auscultation began as early as 1885. They have an electronic apparatus for recording noises and have produced some interesting results from a study of 27 persons, some of whom were normal, while some had arthritis. Where there was no history of joint injury or disease, all was silent except for short, sharp sounds corresponding to the familiar joint crack or snap. The volume of noise was increased in most cases of disease or previous injury. Where injured or diseased joints were not abnormally noisy, complaint of pain was minimal. The authors consider that this method will supplement clinical examination and produce useful permanent records of progress in joint disease.

—

INTRA-ARTICULAR PHENYLBUTAZONE

Does phenylbutazone have a specific anti-inflammatory effect? This question was investigated by Neustadt and Steinbrocker of New York (*J. Lab. & Clin. Med.*, 47: 284, 1956), who injected the drug on 87 occasions intra-articularly into 33 patients with various disorders of muscle and joint. There was a high proportion of beneficial responses to this procedure. Of 18 patients with rheumatoid arthritis, seven derived major and seven minor benefits. Of 11 patients with osteoarthritis, one showed major improvement and seven slight to moderate improvement. The authors consider that their results strongly suggest some anti-inflammatory effect though the response may be due to a non-specific physico-chemical reaction. They gave the substance in 20% solution, using 3-5 ml. with intervals of one week. No untoward results were seen.

—

PLACEBOS AND HYPERTENSION

Davignon and his colleagues from the Hôtel-Dieu, Montreal, draw attention once more to the power of the placebo. They treated 30 patients with hypertension by means of a daily dose of placebo and found that about 60% claimed improvement. They warn once more against the use of hypotensive drugs, whose effects are yet to be proved, without strict controls. Much money and time will be saved, as well as reputations, if the initial studies of new substances are always made in an objective fashion by qualified research workers.—*Union méd. Canada*, 85: 36, 1956.

LEDERLE STUDENT RESEARCH FELLOWSHIPS

Medical Student Research Fellowships, available to medical schools throughout the United States and Canada, are now being offered for the current year by Lederle Laboratories Division, American Cyanamid Company.

The Fellowships, not exceeding $600 for any one individual, are intended to relieve some of the financial burden of students who desire to devote their summer vacations to basic research in the preclinical medical sciences.

(Continued on page 48)



when neuritis strikes

how long need it last?

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Then, swallow tablet for 4-hour protection with theophylline-ephedrine-phenobarbital.

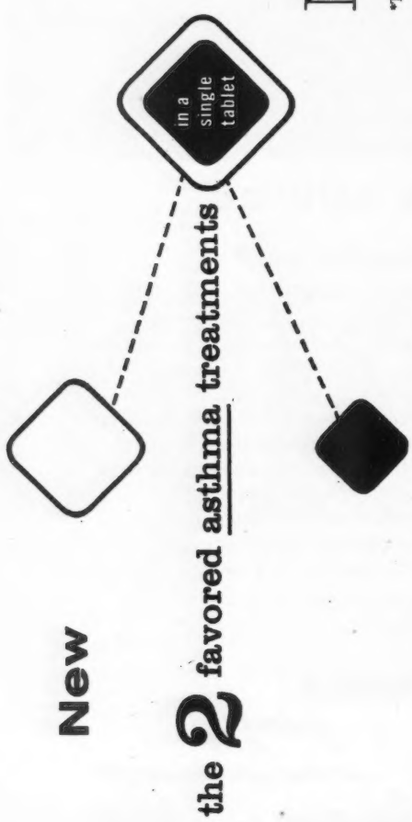
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NEWS AND NOTES

(Continued from page 47)

Selection of students to receive the award will be made by the dean of the medical school or his selection committee. Students who apply must be of good scholastic standing and have the consent of the faculty member under whose supervision their research is to be conducted. Such research may be carried on in another medical school, if the arrangements are satisfactory to faculty authorities in both schools.

AMERICAN COLLEGE OF CHEST PHYSICIANS

The 22nd Annual Meeting of the American College of Chest Physicians will be held at the Hotel Sherman, Chicago, Illinois, June 6 through 10, 1956. The scientific programme will include prominent speakers on all aspects of heart and lung diseases. In addition to formal presentations, there will be a number of symposia, round table luncheon discussions, seminars, and motion pictures.

The Fireside Conferences, which were inaugurated at the annual meeting of the College in 1955 and proved to be so popular, will be repeated. At this session, more than 50 experts will be present to lead the discussions on many subjects of current interest in the specialty of diseases of the chest.

Examinations for Fellowship in the College will be held on Thursday, June 7. On Saturday evening, June 9, more than 150 physicians will receive their certificates of Fellowship at the annual Convocation, which will precede the Presidents' Banquet.

All interested physicians are cordially invited to attend the 22nd Annual Meeting of the College; there is no registration fee. Copies of the programme may be obtained by writing to the Executive Offices, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

WHO EXECUTIVE BOARD

The 17-day meeting of the Executive Board of the World Health Organization ended early in February in Geneva. The principal decisions were as follows: the health programmes for 1957 submitted by Dr. M. G. Candau were approved, but his budget was cut from $11,400,000 to $11,000,000. Some new activities will therefore be deleted. A suggestion by the United States to cut the budget further was not adopted. The Board welcomed the information by the Soviet Deputy Minister of Health that the U.S.S.R., which ceased active participation in the work of WHO in 1948, was prepared to assist actively once more, and also to make some arrangements for settling its outstanding financial commitments. Since resumption of active participation by the U.S.S.R. and possibly other European countries seems likely in the near future, and additional financial contributions may therefore be forthcoming, permission was given by the Board to increase the budget to be presented to the Assembly in May. The Board was pleased to note that the U.N. technical assistance programme, which will yield to WHO over $5,000,000 this year, is now in a more stable financial position.

The Board approved the WHO programme for studies on various medical aspects of atomic energy, including protection of health against radiations, effect of radiations on human heredity, standardization of measurements for radiation, and co-ordination of research. WHO is to study the possibility of creating registry centres for study of cancer tissues in various parts of the world and is also to co-ordinate a vigorous programme of research on resistance to modern pesticides, an alarming feature of recent mass campaigns against disease. A five-member committee on malaria eradication was appointed to advise the Director General. Increased action against leprosy was urged, and WHO was asked to increase its assistance in the mental health field.

The new representative of the United States on the Executive Board is Dr. Frederick J. Brady, Assistant Chief of the Division of International Health, U.S. Public Health Service, who was recently appointed to this position by President Eisenhower, and has a long acquaintance with the work of WHO. Dr. Brady's alternate will be Dr. Charles W. Mayo of the Mayo Clinic. Canada does not at present have a member on this Board.

(Continued on page 50)

WYDASE SPEEDS

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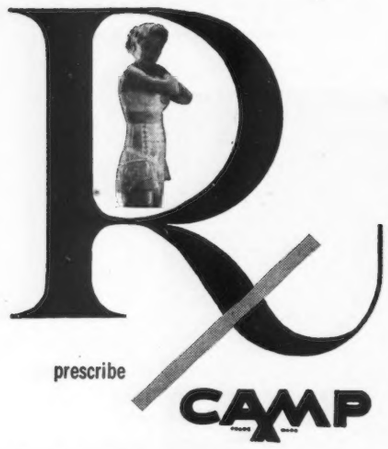
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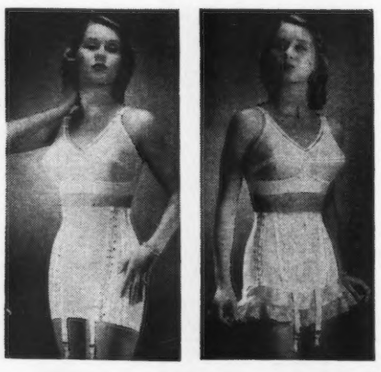
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NEWS AND NOTES

(Continued from page 48)

INTERNATIONAL CHILDREN'S CENTRE

The International Children's Centre, whose headquarters are in Paris, France, describes two courses due to take place at the Centre this year. The ninth course in social pædiatrics designed for physicians will take place from April 9 to July 1, and the curriculum will include all the major questions pertaining to medical social action on behalf of children. One part of this course will take place in France and the rest in another country. Training will be essentially practical with visits to medico-social centres or children's institutes and the course is particularly suitable for physicians carrying out UNICEF and WHO programmes. From September 17 to October 28 there will be a course on problems created by mentally deficient children. These will include lectures, practical work and study circles and will be suitable for psychiatrists, psychologists, educationalists, judges of children's courts and specialist welfare workers.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The office of the Secretary of the American Board of Obstetrics and Gynecology, Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio, announces that the next scheduled examinations (Part II), oral and clinical, for all candidates will be conducted at the Edgewater Beach Hotel, Chicago, Illinois, by the entire Board from May 11 to May 20, 1956. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates.

Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible.

AMERICAN TRUDEAU SOCIETY

Seven special lectures, eight panel discussion on subjects of immediate interest in pulmonary disease management, and 11 sessions of scientific papers have been planned for the 51st Annual Meeting of the American Trudeau Society (the medical section of the National Tuberculosis Association), to be held at the Statler Hotel in New York City, on May 21-23. The programme will cover a wide range in chest diseases, including special lectures on chronic bronchitis, air pollution of cities, pulmonary manifestations of systemic lupus erythematosus, and recent virus research in relation to pulmonary disease.

Reservation blanks for local events may be obtained by writing the National Tuberculosis Association, 1790 Broadway, New York 19, N.Y.

FEDERAL HEALTH GRANTS

Quebec.—Two hospitals of the province will share federal health grants totalling $102,210 to assist in their building programmes. The Foyer Dieppe, an institution for epileptics at St. Hilaire, Rouville County, has been awarded a grant of $56,710 to help provide accommodation for 42 additional patients. At St. Jerome, Terrebonne County, a grant of $45,500 goes towards the construction of a nurses' residence at the Hôtel Dieu hospital.

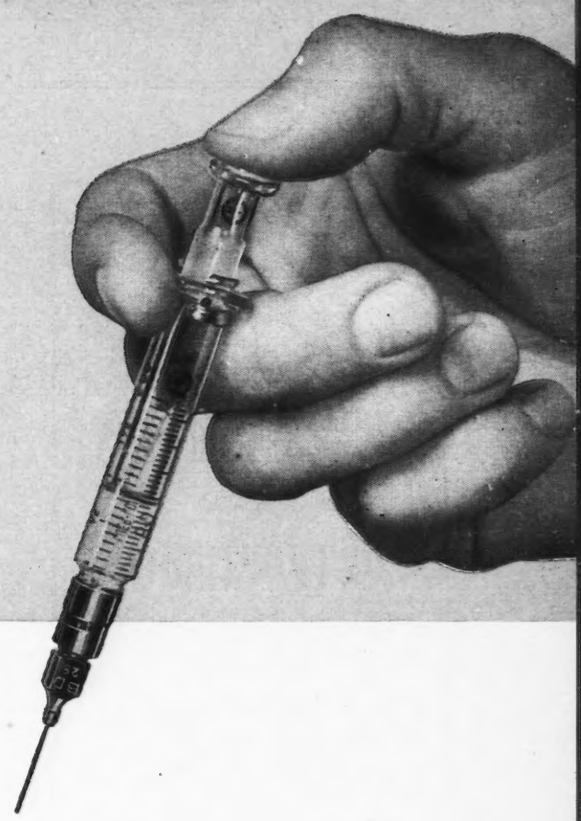
Newfoundland. — Three Newfoundland hospitals will share federal health grants worth $17,040 to assist them in construction and expansion programmes. At Roddickton, a grant of $10,040 goes to the International Grenfell Association Hospital. The money will help meet construction costs of a building with accommodation for six patients, four bassinets, outpatient treatment and dispensary facilities and staff quarters. The new hospital will provide services for some 2,500 persons in the Roddickton and Canada Bay area. A grant of $3,000 will assist in construction costs of an extension to the Hamilton Valley Nursing Station. In St. John's a grant of $4,000 goes to St. Clare's Mercy Hospital to help provide equipment needed to improve facilities for child and infant care.

SCHOLARSHIPS IN ANÆSTHESIOLOGY

International scholarships in anæsthesiology for women physi-

(Continued on page 52)

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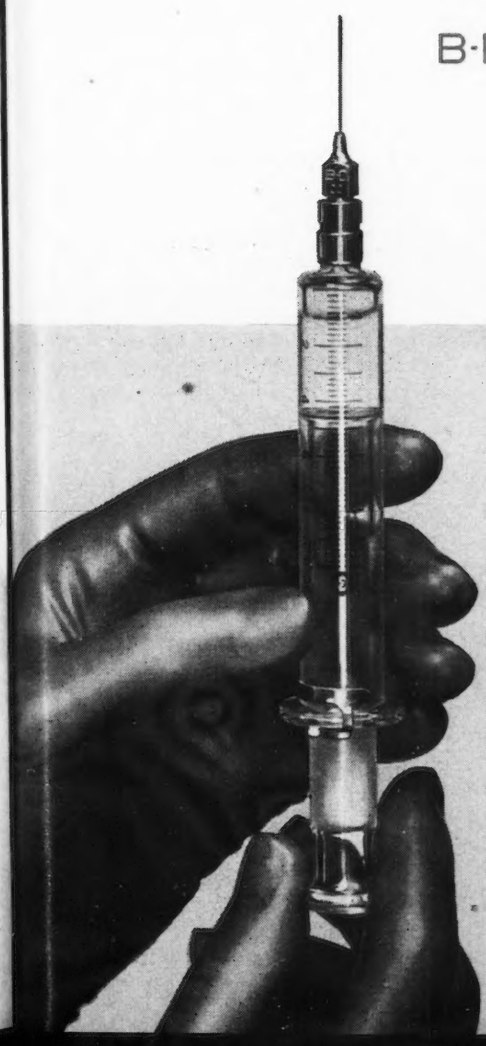
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NEWS AND NOTES

(Continued from page 50)

cians have been established at the New England Hospital, Boston, Massachusetts. The Department is approved for the required two-year residency training.

Candidates from English-speaking countries are eligible for a scholarship which includes a stipend of $1,800 a year, plus full maintenance and travel expenses to the New England Hospital, from the place of residence. Return passage is guaranteed provided the resident returns to her country immediately after her training at the hospital is over. In order to qualify, an applicant must be a graduate of an approved medical school and must have had a minimum of one year's approved internship. Both diplomas must have been received in an English-speaking country.

In awarding the scholarships, character, scholastic ability and the intention of practising in the specialty of anæsthesiology will be taken into consideration. Application blanks and further information may be obtained from the Executive Director, New England Hospital, Columbus Avenue and Dimock Street, Boston 19, Massachusetts, U.S.A.

CANCER QUACKERY

In an editorial in the Canadian Cancer Society Newsletter, the subject of cancer quackery is well summarized. The editor says:

"A Commission set up by the California Medical Association to study their practices says a quack usually has one or more of the following characteristics:

"1. His treatment is available only from himself.

"2. His treatment bears his own name or that of a high-sounding research organization.

"3. His treatment is advertised.

"4. He claims he is being persecuted by the 'Medical Trusts.'

"5. His 'cured' patients and greatest supporters have only his word for it that they had cancer in the first place.

"6. He discourages or refuses consultations with reputable physicians.

"To these, two other characteristics may be added. First, the descriptive literature is very convincing to the layman. The one who thinks that he couldn't be fooled does not realize just how logical the treatment may be made to seem.

"Secondly, the treatments are almost always simple. No painful operations, no prolonged stays in hospital are necessary. All that is required is a daily application of a salve to the skin, a regular dose of medicine or an injection. The medicines and injections most often consist of harmless ingredients."

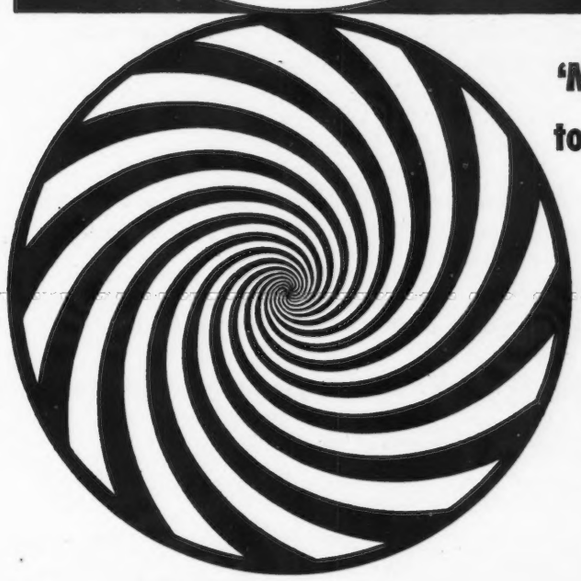
AERO MEDICAL ASSOCIATION

The Annual Meeting of the Aero Medical Association will be held at the Drake Hotel, Chicago, Illinois, on April 16, 17, and 18. This year's meeting will provide a comprehensive review of current progress in aviation medicine. There will be 137 papers dealing with every aspect of the field and coming from military and civilian sources in nine countries. Of particular interest will be the section meetings, which will include in their agenda panel discussions of vital topics by authorities in each field. The sections convening will include the following sub-specialties: Space Medicine, Civil Aviation Medicine, Aviation Physiology, Aviation Ophthalmology, Acceleration and Deceleration, Air Passenger Transportation, Noise and Vibration, Pilot Selection and Aviation Psychology, Personal Equipment, Aviation Pathology, Aviation Medical Education, and a combined symposium on Escape from High Performance Aircraft. All members of the profession are cordially invited to attend any or all of these sessions.

COURSES IN PÆDIATRICS

The following short courses will be conducted at the Children's Hospital of Philadelphia in May and June 1956. (1) *Pediatric Advances for Pediatricians and General Practitioners.* May 28 to June 1, 1956; (2) Practical Pediatric Hematology. June 4, 5 and 6; (3) Blood Group Incompatibilities and Erythroblastosis Fetalis. June 7 and 8. For information write to Irving J. Wolman, M.D., Children's Hospital of Philadelphia, 1740 Bainbridge Street, Philadelphia 46, Pa.





'MARZINE' acts promptly to prevent or relieve . . .

MOTION SICKNESS

NAUSEA AND VOMITING OF PREGNANCY

VERTIGO

RADIATION SICKNESS

POST-OPERATIVE VOMITING

'MARZINE' *brand Cyclizine available as:*

TABLETS*:	50 mg. Scored	Bottles of 100, 500 and 1,000
SUPPOSITORIES*:	100 mg.	Boxes of 12
INJECTION†:	50 mg. in 1 c.c.	Boxes of 12 and 100

**Cyclizine Hydrochloride*
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Full information will be sent on request.



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Essential B vitamins to relieve complicating nutritional deficiencies.

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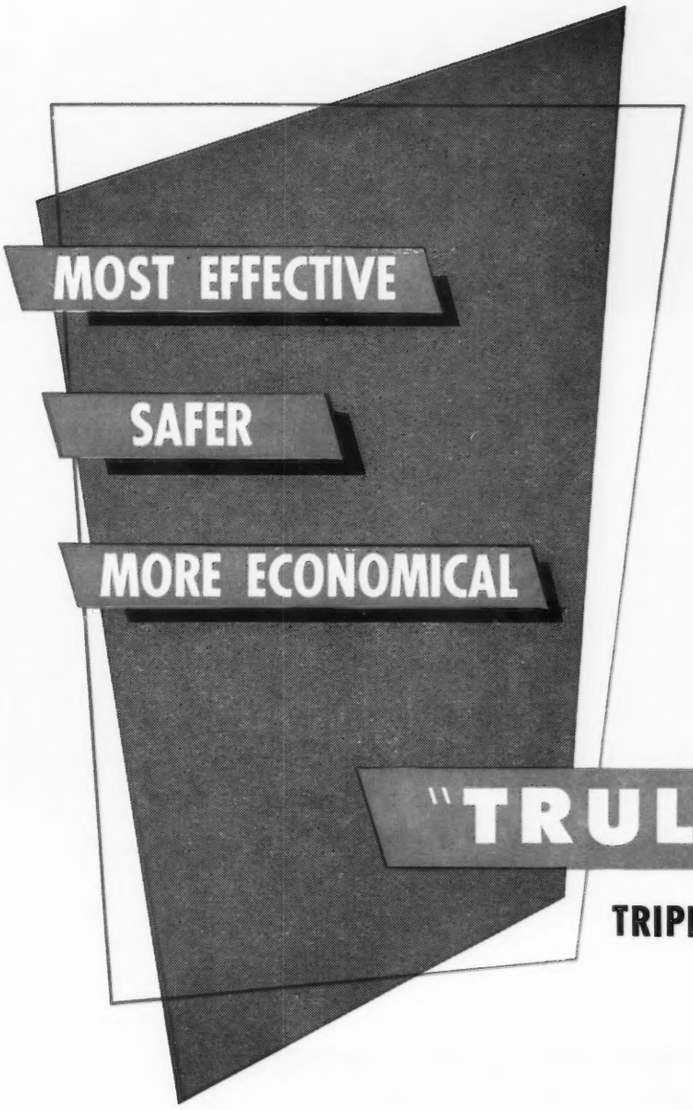
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*Mol-Iron is an exclusive, patented, coprecipitated complex of ferrous and molybdenum salts which exhibits unique advantages as a hemopoietic agent.

**as derived from Streptomyces fermentation extractives.

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TRIPLE SULFAS and PENICILLIN

BROAD SPECTRUM OF ACTIVITY achieved by a two-pronged attack on infecting organisms. In urinary tract infections, as in most other infections ". . . duration of treatment was considerably shortened with combined chemo and antibiotic therapy."*

VIRTUAL FREEDOM FROM REACTIONS as compared with such broad spectrum antibiotics as oxytetracycline, chlortetracycline and tetracycline.

Fungal overgrowth, especially by monilia, — a very real danger — does not occur.

About half the price of many antibiotics.

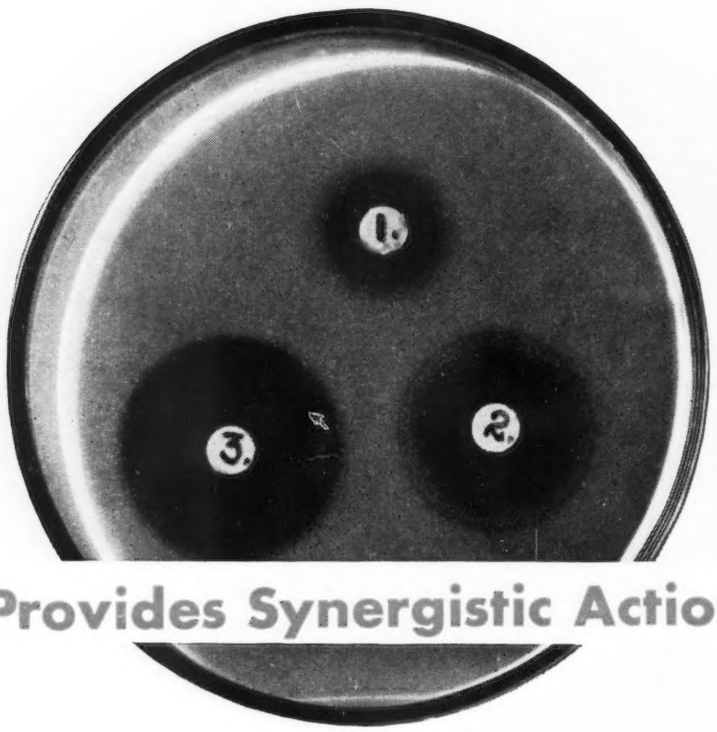
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MONTREAL CANADA

* Lingard, W. F., The Treatment of Urinary Tract Infections. Canad. M.A.J., 74:353, 1956.

SEE FOLLOWING PAGES FOR COMPLETE LIST OF FORMULAE FOR CHILDREN AND ADULTS

"TRULFACILLIN"

TRIPLE SULFAS and PENICILLIN



STAPH. AUREUS No. 209

1. Inhibitory zone produced by disc impregnated with 1.0 mg. triple sulfonamides.
2. Inhibitory zone produced by disc impregnated with 0.5 unit of penicillin-G.
3. Inhibitory zone produced by disc impregnated with 1.0 mg. triple sulfonamides plus 0.5 unit of penicillin-G.

Provides Synergistic Action

in the treatment of

PNEUMOCOCCIC, STAPHYLOCOCCIC, GONOCOCCIC
and
HEMOLYTIC STREPTOCOCCIC INFECTIONS

•

SCARLET FEVER, OTITIS MEDIA, TONSILLITIS,
VINCENT'S ANGINA and URINARY TRACT INFECTIONS

•

and for the prevention of
SECONDARY INFECTIONS
during
INFLUENZA, MEASLES, WHOOPING COUGH

Frosst

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"TRULFACILLIN"

TABLETS

Each tablet contains:

Sulfamethazine..... 167 mg.
Sulfadiazine..... 167 mg.
Sulfamerazine..... 167 mg.
} 7½ gr.

Crystalline potassium penicillin-G...
- **100**,000 I.U. — "TRULFACILLIN" 7½-100
- **150**,000 I.U. — "TRULFACILLIN" 7½-150
- **300**,000 I.U. — "TRULFACILLIN" 7½-300

DOSE: One or two tablets every 4 to 6 hours. Trulfacillin tablets should be administered one-half hour before or two hours after meals.

Boxes of 12 tablets. Each tablet is sealed in foil.

SUSPENSIONS

Each 5 cc. teaspoonful contains:

Sulfamethazine..... 167 mg.
Sulfadiazine..... 167 mg.
Sulfamerazine..... 167 mg.
} 7½ gr.

Benzathine penicillin-G.....
- **100**,000 I.U. — "TRULFACILLIN" 7½-100
- **150**,000 I.U. — "TRULFACILLIN" 7½-150
- **300**,000 I.U. — "TRULFACILLIN" 7½-300

DOSE: One to two teaspoonfuls every 4 to 6 hours.

Bottles of 60 cc.

"TRULFACILLIN" PEDIATRIC

SUSPENSIONS

Each 5 cc. teaspoonful contains:

Sulfamethazine..... 65 mg.
Sulfadiazine..... 65 mg.
Sulfamerazine..... 65 mg.
} 3 gr.

Benzathine penicillin-G.....
- **100**,000 I.U. — "TRULFACILLIN" PEDIATRIC 3-100
- **200**,000 I.U. — "TRULFACILLIN" PEDIATRIC 3-200

DOSE: Infants and children — one teaspoonful per 4 pounds of body weight per day in divided doses, e.g., child weighing 8 lb. — ½ teaspoonful every 6 hours; child weighing 16 lb. — 1 teaspoonful every 6 hours.

Bottles of 60 cc.

CAUTION

While untoward effects associated with sulfonamide therapy are greatly reduced by the use of Trulfacillin preparations, vigilance should not be relaxed in the search for and recognition of agranulocytosis, fever, joint pains, skin reactions, etc. In rare instances the injection of penicillin, and more rarely still its oral administration, may cause acute anaphylaxis. The reaction appears to occur more frequently in patients with bronchial asthma and other allergies, or in those who have previously demonstrated sensitivity to penicillin.

Charles E. Frosst & Co.
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WHERE SULFONAMIDES ALONE ARE INDICATED

TRIPLE SULFONAMIDE COMBINATIONS *that provide* EFFECTIVENESS WITH MINIMAL HAZARD

in

PNEUMOCOCCIC, STAPHYLOCOCCIC, MENINGOCOCCIC, GONOCOCCIC and HEMOLYTIC STREPTOCOCCIC INFECTIONS

SCARLET FEVER • MEASLES
OTITIS MEDIA • TONSILLITIS
VINCENT'S ANGINA • MENINGITIS
URINARY TRACT INFECTIONS

"TRULFA"

SUSPENSION

Each 5 cc. teaspoonful contains:

Sulfathiazole.....	167 mg.	7½ gr.
Sulfadiazine.....	167 mg.	
Sulfamerazine.....	167 mg.	

in a pleasantly flavoured suspension.

TABLET

Each scored tablet contains:

Sulfathiazole.....	167 mg.	7½ gr.
Sulfadiazine.....	167 mg.	
Sulfamerazine.....	167 mg.	

"TRULFA" and "TRULFA-ZINE" provide high solubility in urine with virtual freedom from sulfonamide crystalluria, and greatly reduced sensitivity through the use of triple sulfonamides.[1]

[1]Lehr, David, "Present Status of Sulfonamide Therapy", Scientific Exhibit, Annual Convention A.M.A., San Francisco, 1954.

"TRULFA-ZINE"

SUSPENSION

Similar in formula to Trulfa Suspension, except that sulfamethazine is used instead of sulfathiazole.

TABLET

Similar in formula to Trulfa Tablet, except that sulfamethazine is used instead of sulfathiazole.

DOSAGE

SUSPENSIONS

Infants and Children: ½ teaspoonful (2.5 cc.) for each 4 pounds of body weight per day in divided doses (approximately 1 grain per pound of body weight) e.g. Child's weight—24 pounds: 1 teaspoonful 3 times daily.
Adults: 2 to 4 teaspoonfuls in water every 4-6 hours.

Bottles of 16 fluid ounces.

TABLETS

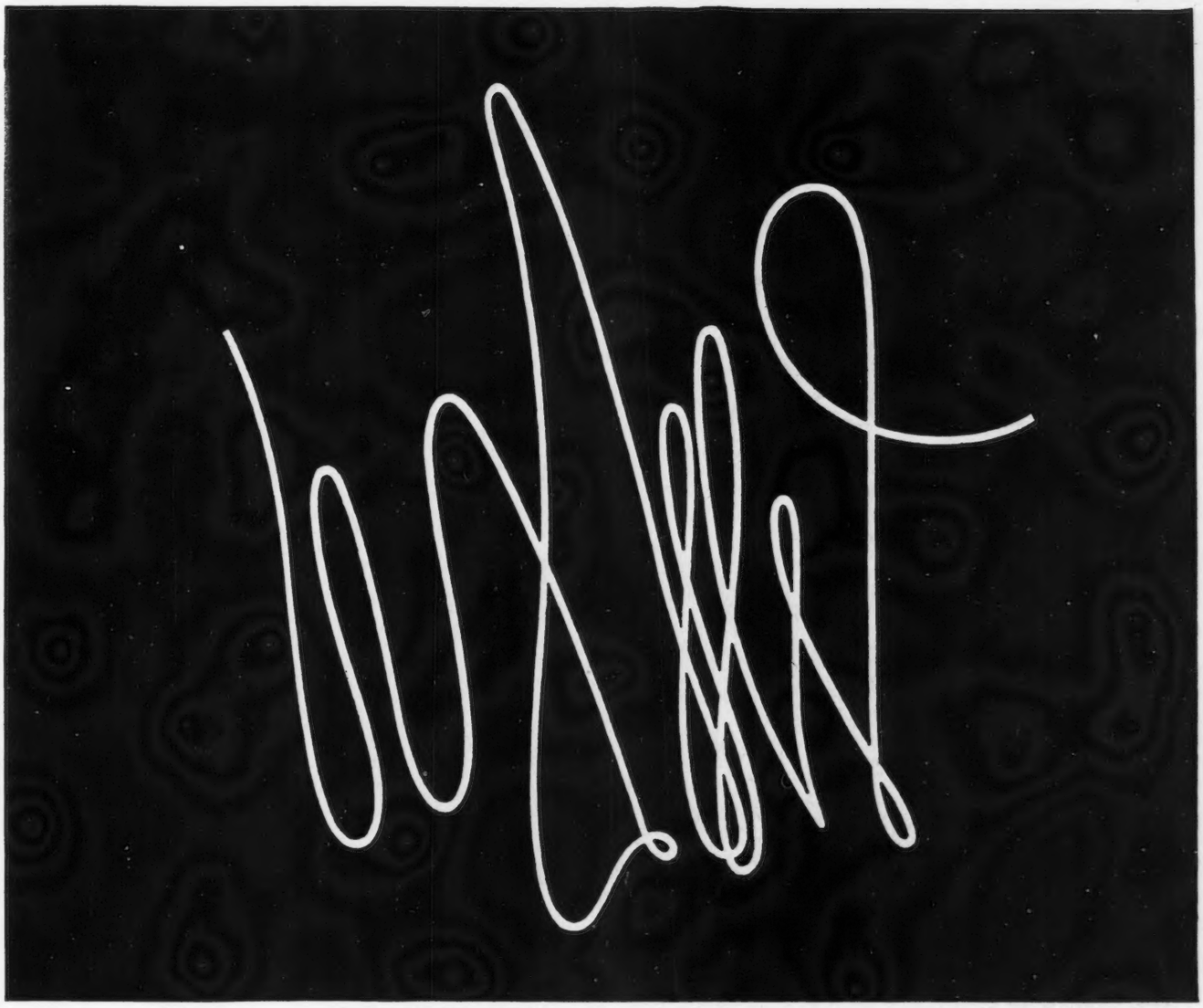
1 to 2 tablets every four to six hours.

Bottles of 100.

CAUTION

While untoward effects associated with sulfonamide therapy are greatly reduced by administration of Trulfa and Trulfa-Zine preparations, vigilance should not be relaxed in the search for and recognition of agranulocytosis, fever, joint pains, skin reactions, etc.

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always an unmistakable pattern . . .

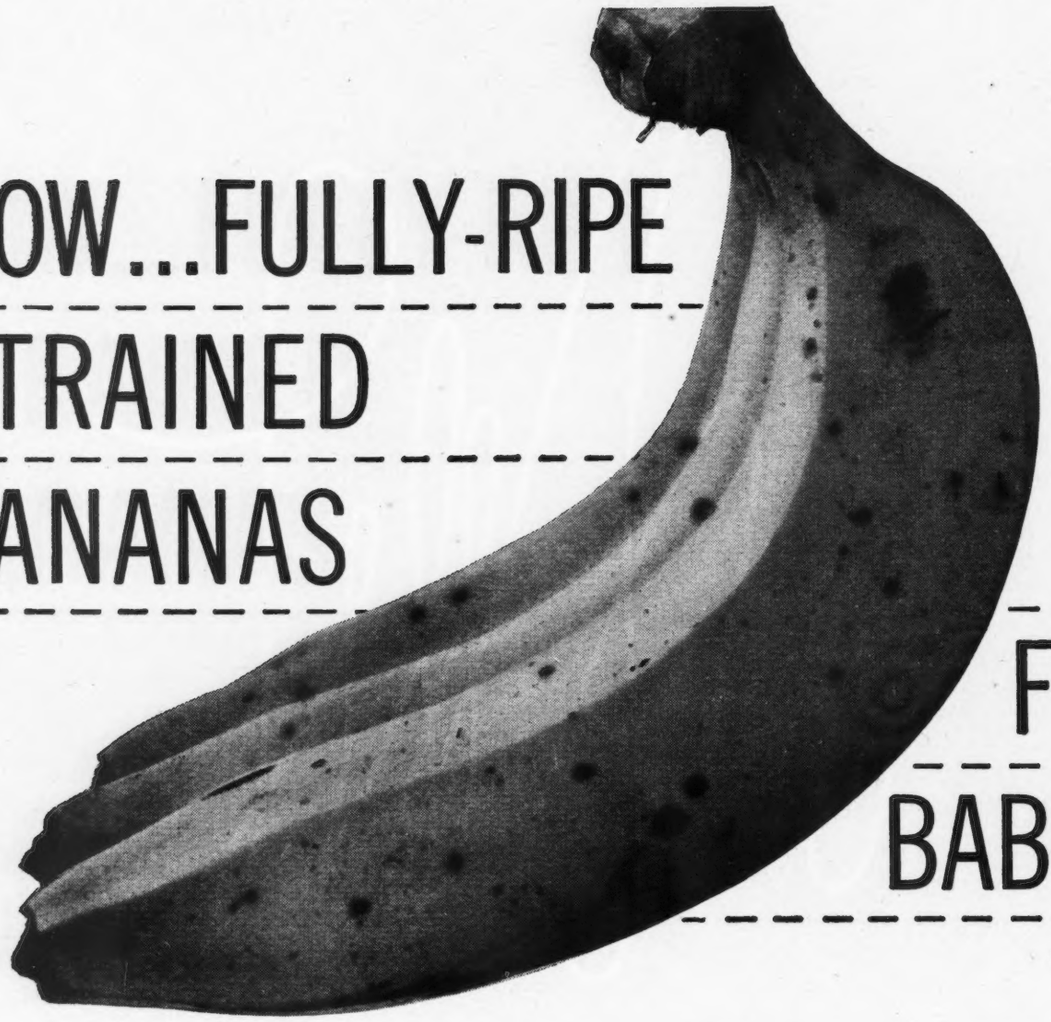
. . . from any angle. Cannot be confused with

bone structure or artifacts on the X-ray plate.

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NOW...FULLY-RIPE STRAINED BANANAS FOR BABIES



Easily Digested! Recognizing the importance of digestibility, Gerber uses only fully ripe fruit for their new Strained Bananas for babies. Degree of ripeness is always uniform. A touch of tapioca is added for stability. Easily digested carbohydrates are derived mainly from the fruit sugar of fully ripe banana puree.

Highly palatable! Gerber Strained Bananas contain a minimum of added sugar for palatability . . . a small amount of lemon juice to enhance flavor and protect appealing banana color.

Pleasant consistency! Extra-smooth texture makes Gerber Strained Bananas particularly agreeable to infants.

Pre-tested! Gerber Strained Bananas are the result of almost 9 years research and laboratory testing, including 133 separate experiments plus consumer preference tests.

NEW EXCLUSIVE! More good-tasting Gerber Strained Foods specially developed for babies

Mixed Fruit. Blend of apples, pears, peaches and pineapple—touched with farina for texture.

Beef Noodle—Hearty combination of potatoes, beef, carrots, noodles—good source of carbohydrates and protein.

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Chicken Noodle—Delicate, easily digested mixture of chicken, noodles, carrots and natural chicken broth.

Chicken Rice—Chicken broth, potatoes, chicken and carrots with a rice flour base.

Above also available in Junior Foods for tots with a few teeth.

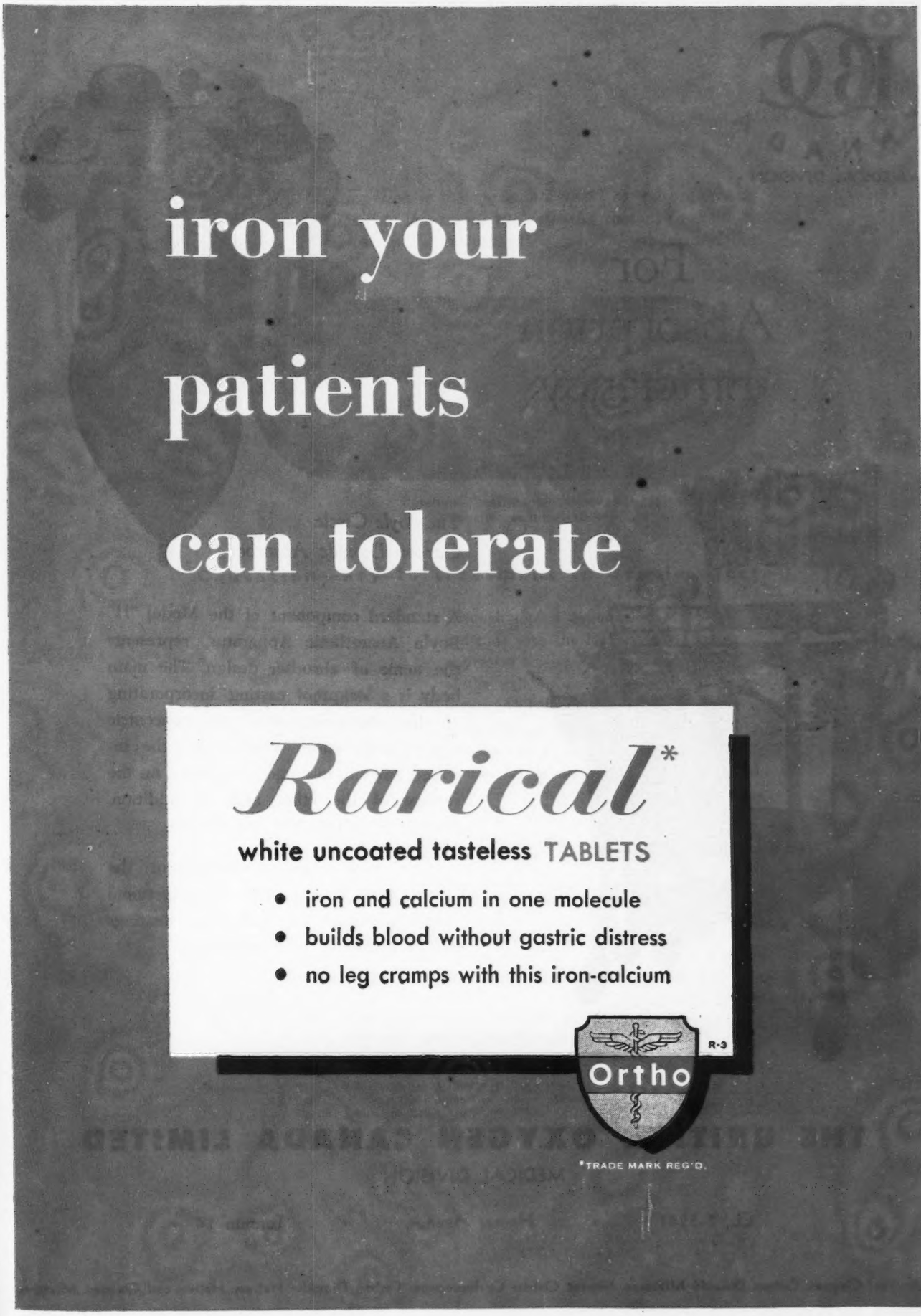
Babies are our business...our only business!

Gerber BABY FOODS

Niagara Falls, Canada

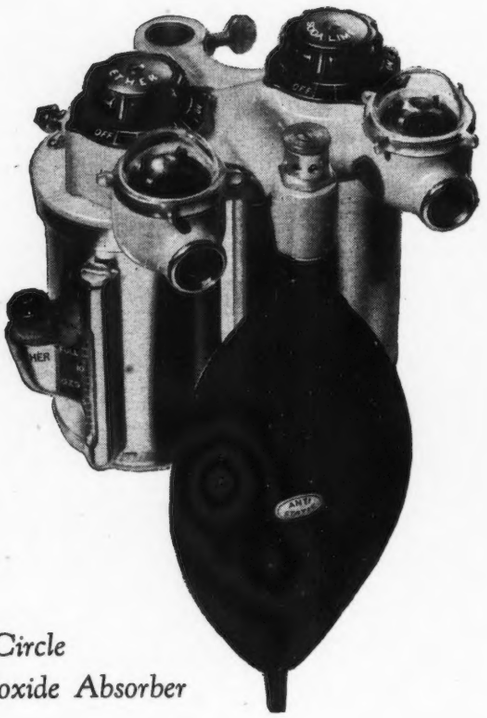


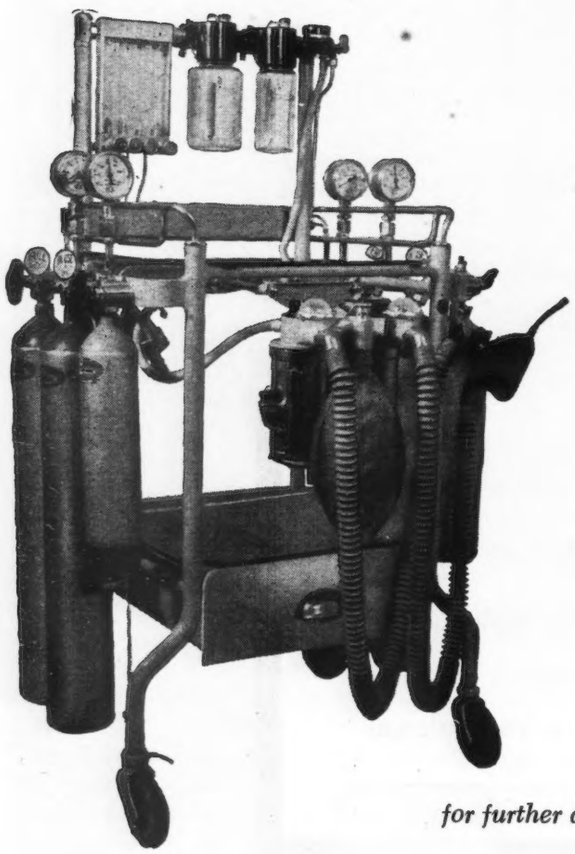
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The Boyle Circle Carbon Dioxide Absorber

A standard component of the Model "H" Boyle Anaesthetic Apparatus, represents the acme of absorber design. The main body is a leakproof casting, incorporating an ether vapourizer fitted with concentric copper baffle tubes which cause the inspired gases to impinge many times on the surface of the ether and, in addition, ensure maximum heat conduction.

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". . . the gastric secretion is the immediate agent of mucosal tissue digestion. . . . Opposed to this stands the defensive factor . . . the two-component mucous barrier"[1] *(the protecting layer of mucus and the mucosal epithelium).*



Rotational gastroscopic views showing coating effect 1½ hours after administration of Amphojel.[2]

Causation—key to treatment in peptic ulcer

Through topical action alone, AMPHOJEL contends with the local causes of ulcer — aggressive acidity coupled with impairment of the wall defenses. Providing a dual approach, AMPHOJEL combines two aluminum hydroxide gels, one reactive, one demulcent. The reactive gel combats the attacking factor in ulcer by promptly buffering gastric acid. The demulcent gel promotes healing of the denuded mucosa by forming a viscous, protective coagulum.

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Supplied: Amphojel Plain — bottles of 12 fl. ozs. and 1 Imp. Gal.
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Amphojel with Mineral Oil — bottles of 12 fl. ozs. and 1 Imp Gal.
Amphojel Tablets — bottles of 50 and 500

References:
1. Hollander, F.: Arch. Int. Med. 93:107 (Jan.) 1954.
2. Deutsch, E.: Scientific Exhibit, Gastroscopy, Clinical Meeting A.M.A., St. Louis, December, 1953.

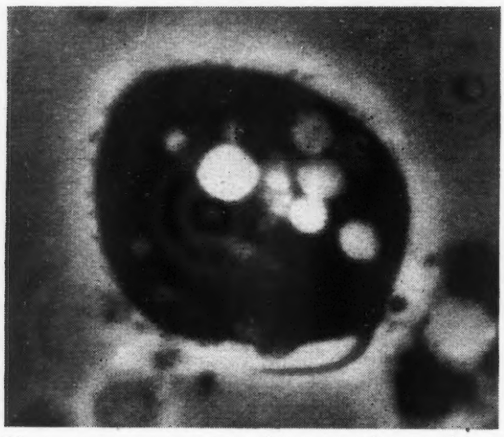
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DAVIS TECHNIQUE USING VAGISEC* JELLY AND LIQUID EXPOSES AND EXPLODES TRICHOMONADS HIDDEN AWAY IN RUGAE



Phase-contrast microscope shows a trichomonad in a mucinous vaginal smear.

MANY trichomonacides failed in years past largely because they reached only the parasites swimming freely in the vaginal canal—not those hiding under epithelial cells deep among the vaginal rugae. In fact, some agents actually coagulated the albuminous material lining the surface and protected the trichomonads![1]

Success at last. Today, however, you can overcome this problem because VAGISEC jelly and liquid quickly penetrate to trichomonads' hideaways. You can now treat vaginal trichomoniasis successfully, using the Davis technique. Carl Henry Davis, M.D., eminent gynecologist and author, and C. G. Grand, research physiologist, introduced VAGISEC liquid as "Carlendacide" and had it tested by over 100 well-known obstetricians and gynecologists. Dr. Davis states, ". . . over 90% of apparent cures have been obtained. . . ."[2]

Overpowering action. Three surface-acting chemicals in VAGISEC liquid, acting synergistically, not only reach trichomonads but explode them![3] A chelating agent complexes and removes the calcium of the calcium proteinate. A wetting agent removes lipid materials. A detergent denatures the protein. The parasites imbibe water, swell and explode.

The Davis technique.† Dr. Davis recommends a combination of office treatments and home treatments, using both VAGISEC jelly and liquid in home treatments. "A few women have infected cervical, vestibular or urethral glands and require other types of treatment. . . ."[2] It is well to remember the role of the male as carrier of the organism and prescribe protection against re-infection from the husband.[2]

Office treatment. Expose vagina with speculum. Wipe walls dry with cotton sponges and wash thoroughly for about three minutes with a 1:250 dilution of VAGISEC liquid. Remove excess fluid with cotton sponges. Dr. Davis recommends six office treatments, three the first week, two the second, and one the third.

Home treatment. Patient inserts VAGISEC jelly each night and douches with VAGISEC liquid (2 teaspoonfuls in 2 quarts of warm water) each morning except on office treatment days, through two menstrual periods. Continued douching two or three times a week helps to prevent re-infection. Pregnant women should have office treatments only.

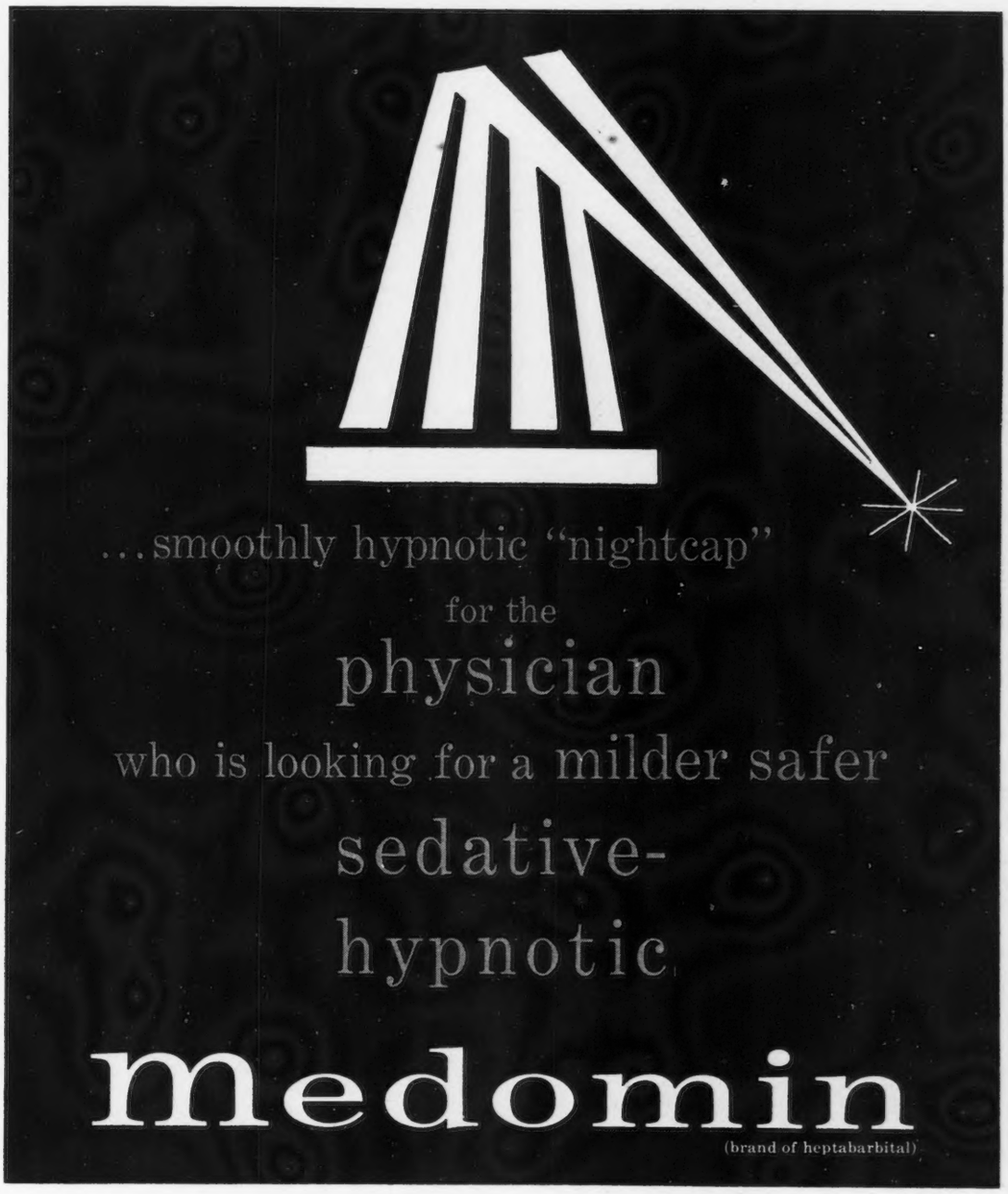
Summary. The unique synergistic action of three agents comprising VAGISEC liquid reaches and explodes hidden as well as surface trichomonads. This therapy has a high rate of success and results in fewer flare-ups. VAGISEC jelly and liquid are non-toxic and non-irritating, and leave no messy discharge or stain.

*Trade-mark †Pat. App. for

JULIUS SCHMID (Canada) Ltd.
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Active ingredients: Polyoxyethylene nonyl phenol, Sodium ethylene diamine tetra-acetate, Sodium dioctyl sulfosuccinate. In addition, VAGISEC jelly contains Boric acid, Alcohol 5% by weight.

1. Davis, C. H.: Am. Jour. Obst. & Gynec. *68*:559 (Aug.) 1954.
2. Davis, C. H.: West. J. Surg. *63*:53 (Feb.) 1955.
3. Davis, C. H.: J.A.M.A. *157*:126 (Jan. 8) 1955.



MEDOMIN (brand of heptabarbital):
Tablets of 50 mg., 100 mg. and 200 mg.

Recommended Dosage:
As a hypnotic: 200-400 mg. before retiring
As a sedative: 50-100 mg. two or three times daily

GEIGY PHARMACEUTICALS

Canad. M. A. J.
April 1, 1956, vol. 74



MERATRAN Profile **DELAYED POSTPARTUM DEPRESSION**

Delayed Postpartum Depression

Sex: Female Age: 28 Occupation: Housewife
Chief Complaint: fatigue

Symptoms: crying, fainting spells, marked premenstrual depression.

Observations: two normal births after period of "infertility". Sudden change in household routine too much to cope with.

Treatment: Amphetamine and phenobarbital failed. Meratran given 1 mg. t.i.d. - July 1954. Treatment stopped, symptoms returned. Meratran 1 mg t.i.d. resumed May 1955.

Response: depression relieved.

Results: able to carry on household duties husband said everything was going very smoothly.

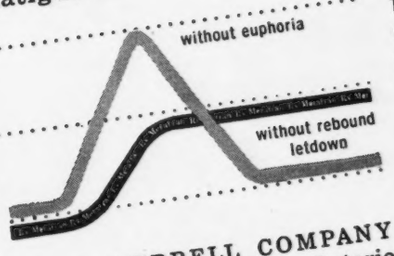
One more case in point for

Meratran

Pipradrol Hydrochloride

in functional fatigue and mild depression

Meratran often restores your emotionally tired and depressed patients to their usual level of alertness, interest and productivity.



In doses individualized to the patient, Meratran produces a subtle, comfortable onset of action, and well-being without jitters or apprehension. May be used over prolonged periods of time. There is no significant effect on blood pressure or respiration, little or no insomnia, or effect on normal appetite, no tolerance or drug habituation; wide range of safety.

Dose: 6 mg. daily, adjusted downward to patient need.

THE WILLIAM S. MERRELL COMPANY
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T.M. 'MERATRAN'

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Since 1828

Another exclusive product of original Merrell research

Case history from the actual files of an eminent physician; photo professionally posed.

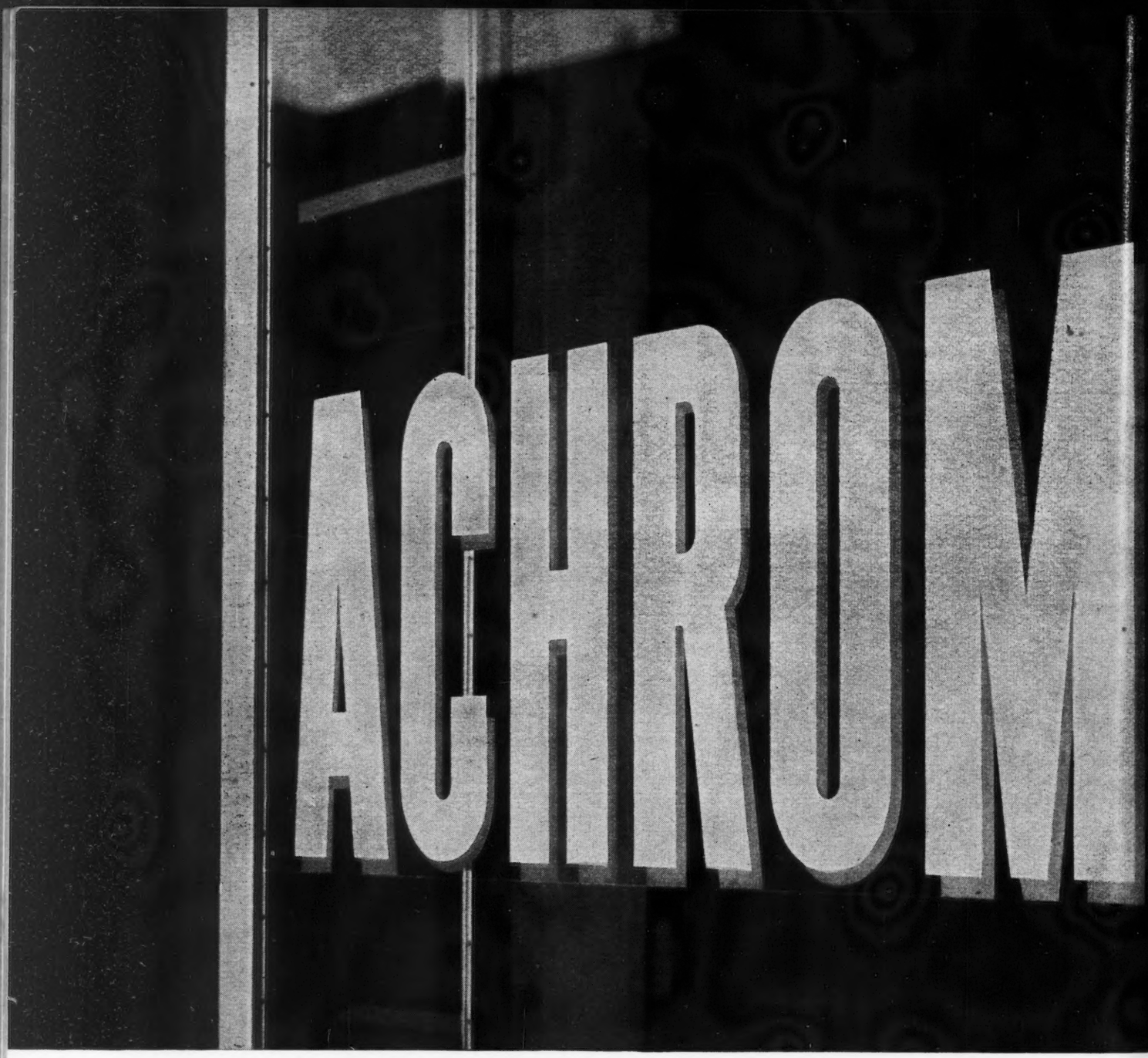


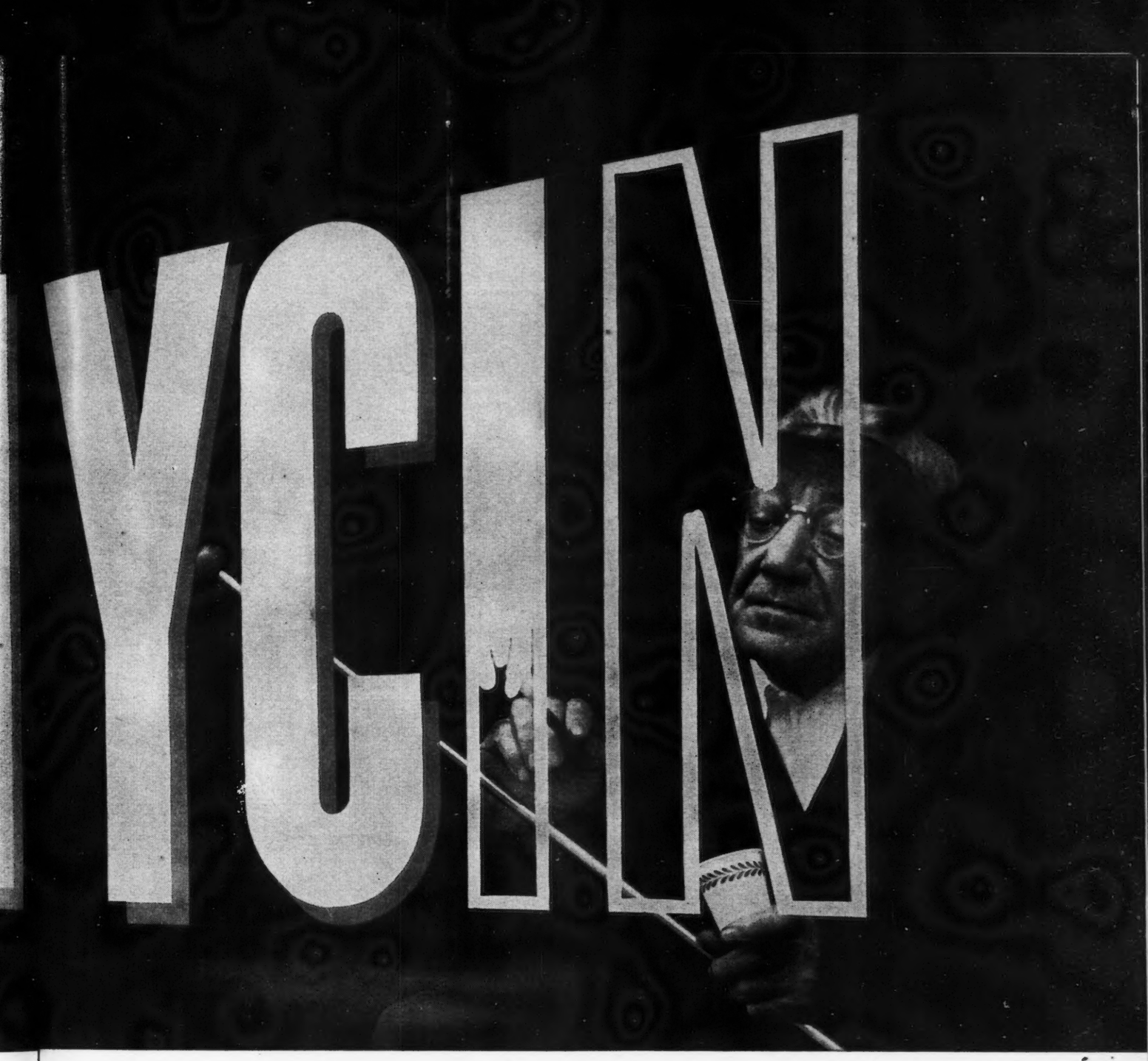
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Tetracycline *Lederle*

widely prescribed because of these important advantages:

1) rapid diffusion and penetration
2) prompt control of infection
3) true broad-spectrum activity (proved effective against a wide variety of infections caused by Gram-positive and Gram-negative bacteria, rickettsiae, and certain viruses and protozoa)
4) negligible side effects
5) every gram produced in Lederle's *own* laboratories under rigid quality control, and offered *only* under the Lederle label
6) a *complete* line of dosage forms



in prolonged illness, prescribe

ACHROMYCIN SF

TETRACYCLINE with STRESS FORMULA VITAMINS

Attacks the infection, bolsters the body's natural defense. Stress vitamin formula suggested by the National Research Council in *dry-filled, sealed* capsules with ACHROMYCIN, 250 mg. Also available: ACHROMYCIN SF ORAL SUSPENSION (Cherry Flavor), 125 mg. per 5 cc. plus vitamins.



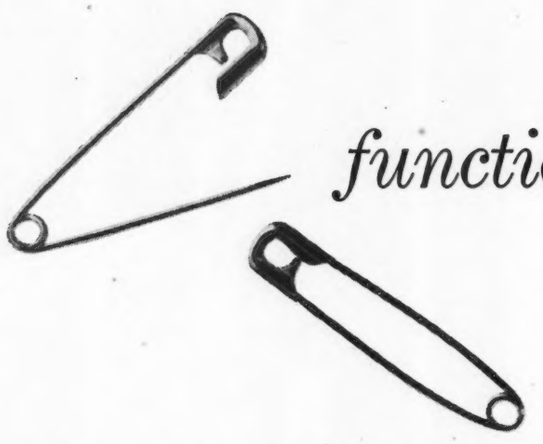
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(a Lederle exclusive!) for more rapid and complete absorption. No oils, no paste, tamperproof!

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. . . as the safety pin, the axe or the oar which, being functionally correct, have never been improved upon. MAGNOLAX is functionally correct in the management of constipation because it is an emulsion of milk of magnesia and liquid petrolatum. Magnolax contains no sugar or fats; it has a pleasant vanilla flavor.

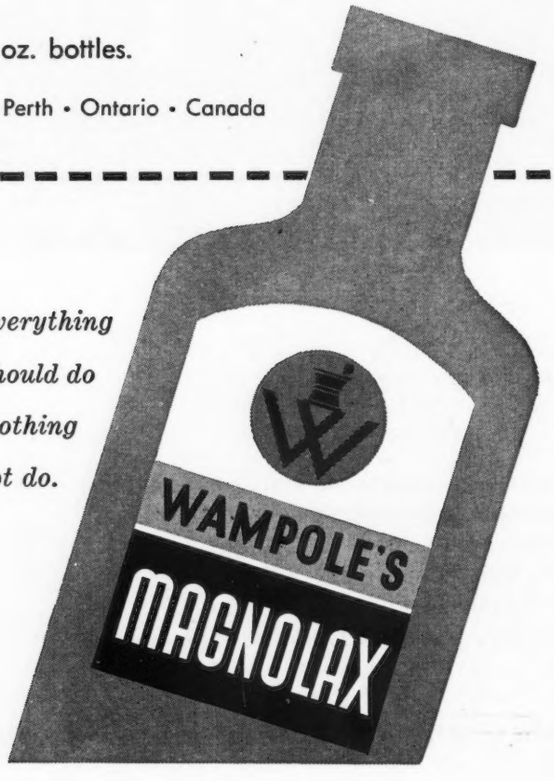
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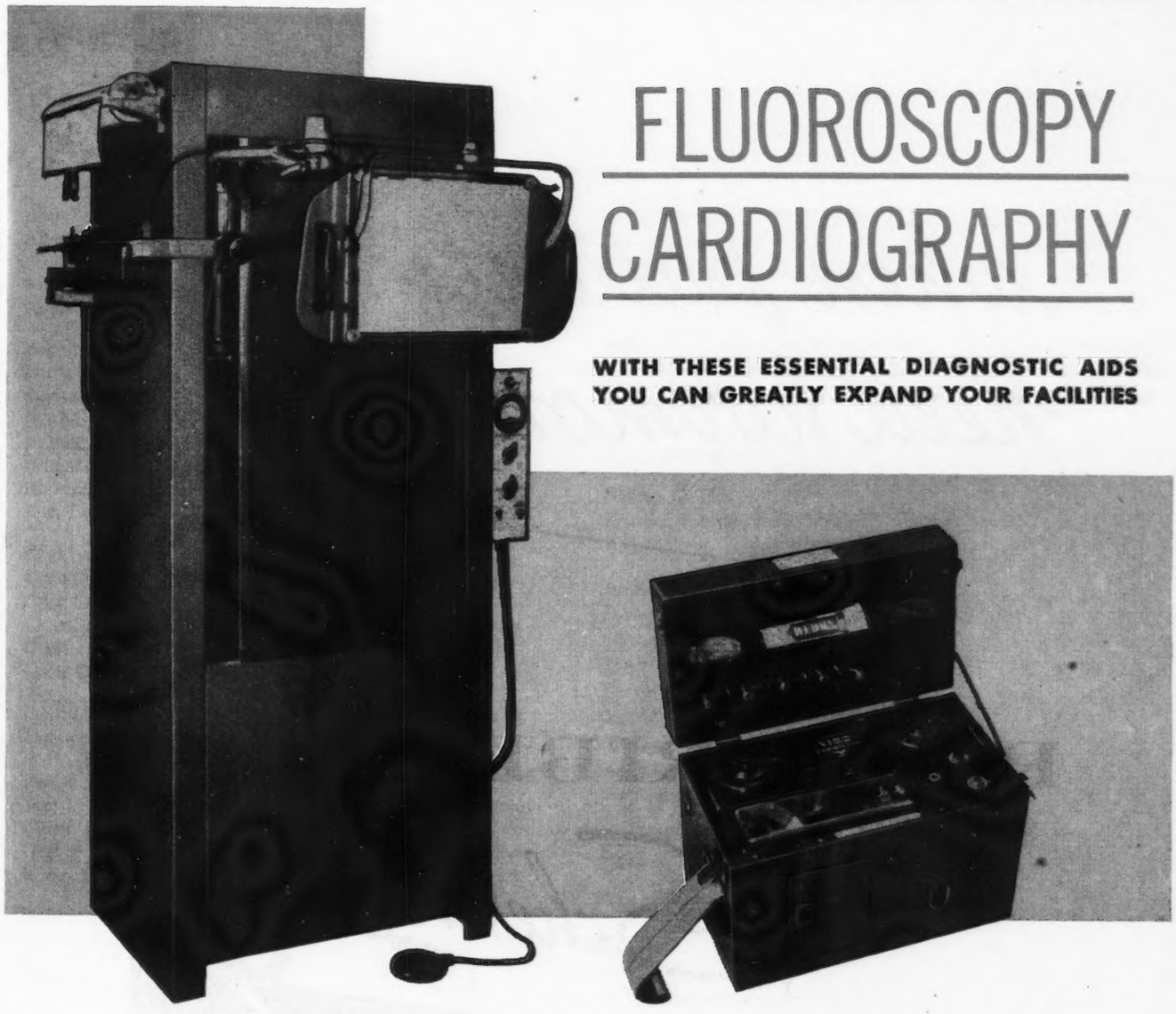
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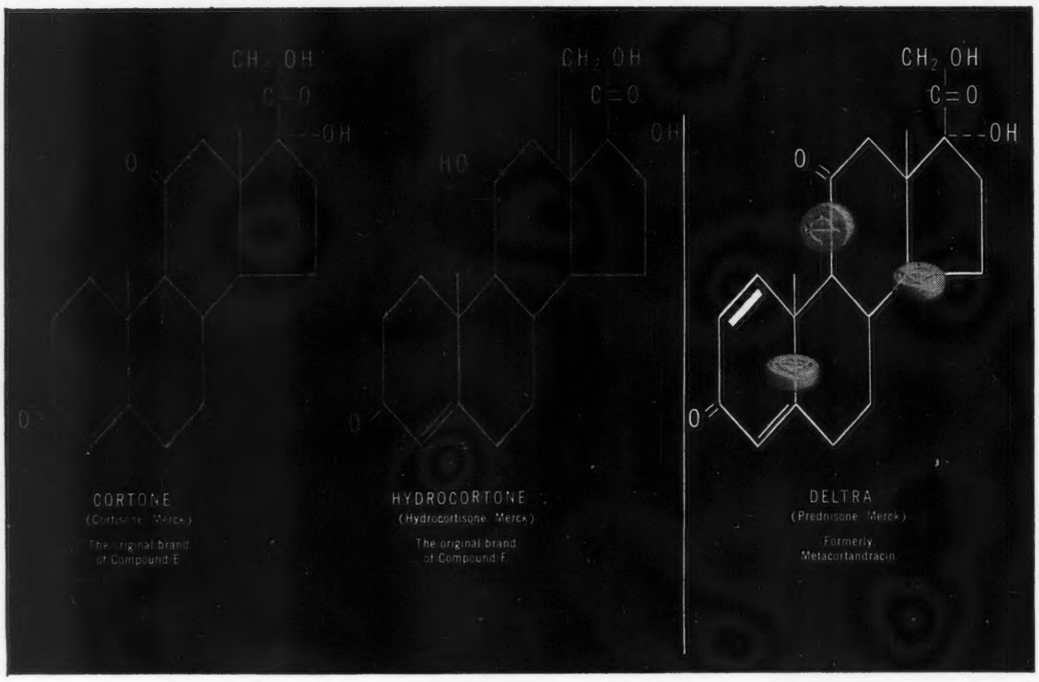
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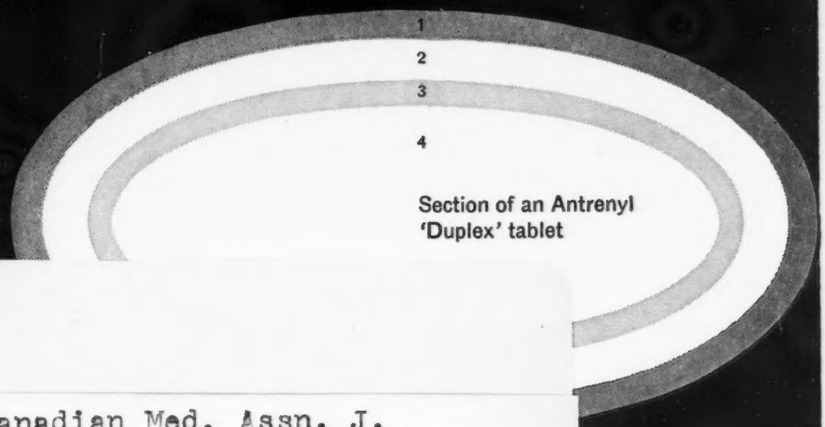
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